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=> d his
     (FILE 'HOME' ENTERED AT 11:35:39 ON 21 MAR 2002)
     FILE 'HCAPLUS' ENTERED AT 11:35:55 ON 21 MAR 2002
            228 S THOMSON B?/AU
L1
L2
           2196 S ALI S?/AU
L3
              5 S MEDCALF N?/AU
              8 S MALTMAN J?/AU
L4
L5
              0 S MALTMAN S?/AU
           2434 S L1-4
L6
L7
              2 S L6 AND DRESSING
                SELECT RN L7 1
     FILE 'REGISTRY' ENTERED AT 11:42:25 ON 21 MAR 2002
L8
             19 S E1-19
     FILE 'HCAPLUS' ENTERED AT 11:43:40 ON 21 MAR 2002
L9
         277593 S L8
L10
            374 S L9(L) DRESSING
L11
            156 S L9(L)WOUND DRESSING
L12
          50264 S HEPARIN OR INOSITOL PHOSPHATE OR FUCOIDIN OR SYNDECAN OR .BET
L13
              8 S L11 AND L12
L14
         120300 S POLYCATION? OR POLYPEPTIDE
              2 S L13 AND L14
L15
              6 S L13 NOT L15
L16
             14 S L10 AND (KERATINOCYTE OR FIBROBLAST)
L17
              4 S L12 AND L17
L18
L19
           2835 S L12(P) (KERATINOCYTE OR FIBROBLAST)
              4 S L19 (P)WOUND DRESSING
L20
              4 S L19 (P) DRESSING
L21
L22
              5 S L19 AND DRESSING
              3 S L22 NOT L16
L23
            181 S L19(L)L14
L24
             0 S L24 AND DRESSING
L25
             20 S L24 AND WOUND
L26
             20 S L26 NOT (L16 OR L22)
L27
             7 S L19(L) POLYLYS?
L28
L29
            467 (POLYLYS? OR L14) (5A) (LAYER? OR COATING)
             0 S L29 AND L11
L30
            156 S L10 AND L11
L31
              8 S L31 AND L12
L32
              2 S L32 AND (KERATINOCYTE OR FIBROBLAST)
L33
L34
           3277 S (POLYLYS? OR L14) (5A) (LAYER? OR COATING OR GEL OR HYDROGEL O
             51 S L34 AND L12
L35
              6 S L35 AND (KERATINOCYTE OR FIBROBLAST)
L36
     FILE 'USPATFULL' ENTERED AT 12:23:13 ON 21 MAR 2002
          18288 S KERATINOCYTE OR FIBROBLAST
L37
           1926 S (POLYLYS? OR L14) (5A) (LAYER? OR COATING OR GEL OR HYDROGEL O
L38
          19953 S HEPARIN OR INOSITOL PHOSPHATE OR FUCOIDIN OR SYNDECAN OR .BET
L39
             22 S L37(P)L38
L40
              2 S L40(P)L39
L41
L42
              0 S L41 AND DRESSING
L43
            255 S L37 AND L38 AND L39
L44
             30 S L43 AND WOUND DRESSING
L45
             21 S L44 AND REVERS?
            944 S L37(P)L39
L46
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L47

L48

58 S L46 AND L38

14 S L47 AND DRESSING

| L49 | 9 | S | L47 AND BANDAGE |
|-----|--------|---|---------------------|
| L50 | 15 | S | L48-49 |
| L51 | 726467 | S | MODULAT? OR REVERS? |
| L52 | 14 | S | L50 AND L51 |

=> d ibib abs ind 1

ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1999:42596 HCAPLUS

DOCUMENT NUMBER:

130:115061

TITLE:

Wound dressing comprising a biodegradable

cell anchoring layer

INVENTOR(S):

Thomson, Brian Mark; Ali, Saad Abdul

Majeed; Medcalf, Nicholas;

Maltman, John; Winter, Sharon Dawn

PATENT ASSIGNEE(S): SOURCE:

Smith & Nephew Plc, UK PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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KIND DATE
        PATENT NO.
                                                                          APPLICATION NO.
                                     ____
                                               -----
                                                                          ______
                                                                                                        _____
                                      A2
        WO 9900151
                                                19990107
                                                                          WO 1998-GB1882
                                                                                                        19980626
                                   A3 19990325
        WO 9900151
              W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
                                   A1 19990119
A2 20000405
                                                               AU 1998-82245 19980626
EP 1998-932298 19980626
        AU 9882245
        EP 989866
               R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                      IE, FI
                                                                          JP 1999-505386
        JP 2002507908
                                       T2
                                                20020312
                                                                                                     19980626
                                                                     GB 1997-13406 A 19970626
PRIORITY APPLN. INFO.:
                                                                                                  A 19971128
                                                                     GB 1997-25209
                                                                                                W 19980626
                                                                     WO 1998-GB1882
```

- A wound dressing which comprises a carrier layer having a AΒ non-adherent to cell layer on a wound facing surface thereof is disclosed. The non-adherent layer has bonded thereto a biodegradable cell anchoring layer which anchors mammalian cells. In use, the degradable layer breaks down releasing the cells into the wound site which are discouraged from reattaching to the dressing by the non-adherent layer. Thus, the dressing can switch from a cell binding state to a state in which the binding of cells is discouraged. Systems, methods of treatment and methods of manufg. the dressing are also disclosed. Opsit IV 3000 polyurethane film was exposed to nitrogen plasma and promptly covered with a thin coat of a soln. contq. 20% ethylene glycol diglycidyl ether (I) and 1% CM-cellulose (II). An aq. soln. of 10 mg/mL-heparin was then sprayed on top of I:II acting and the resulting material was dried at 60.degree. for 5 h, then it was sterilized and stored dry. The above film was immersed in fetal calf serum and a suspension of human keratinocytes. Cells adhered to the film within 4-16 h. Following subsequent in vitro culture, the cells detached from the film and were released into the medium.
- IC ICM A61L015-00
- 63-7 (Pharmaceuticals) CC
- STwound dressing biodegradable polymer animal cell
- Proteoglycans, biological studies

```
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (perlecans; wound dressing comprising biodegradable cell
        anchoring layer)
IT
     Polyethers, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (polyamide-; wound dressing comprising biodegradable cell
        anchoring layer)
ΙT
    Polyethers, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (polyester-; wound dressing comprising biodegradable cell
        anchoring layer)
ΙT
     Polyamides, biological studies
     Polyesters, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (polyether-; wound dressing comprising biodegradable cell
        anchoring layer)
     Transforming growth factor .beta. receptors
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (type III; wound dressing comprising biodegradable cell
        anchoring layer)
    Animal cells
ΙT
    Autotransplant
     Culture media
       Dressings (medical)
     Fibroblast
     Keratinocyte
     Polyvalent anions
        (wound dressing comprising biodegradable cell anchoring
        layer)
IT
     Fluoropolymers, biological studies
     Polyoxyalkylenes, biological studies
    Polysiloxanes, biological studies
Polyurethanes, biological studies
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (wound dressing comprising biodegradable cell anchoring
        layer)
IT
     Pentosans
     Peptides, biological studies
     Proteins (general), biological studies
     Syndecans
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (wound dressing comprising biodegradable cell anchoring
        layer)
ΙT
                                868-77-9
     107-73-3, Phosphocholine
                                            9002-84-0, Ptfe
                                                              9003-01-4,
                                     24937-78-8, Ethylene vinyl acetate
                        9003-05-8
     Polyacrylic acid
     copolymer
                 25322-68-3
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (wound dressing comprising biodegradable cell anchoring
        layer)
                                                            9004-34-6D,
ΙT
     9002-89-5D, Polyvinyl alcohol, hydroxyalkyl derivs.
                                        9004-67-5, Methyl cellulose
     Cellulose, hydroxyalkyl derivs.
                                   9012-36-6, Agarose
                                                         9042-14-2,
     Heparin, biological studies
                      9072-19-9, Fucoidin
                                            25104-18-1, Polylysine
     Dextransulfate
     25191-25-7, Polyvinyl sulfate
                                     38000-06-5, Polylysine 68247-19-8,
     Inositol phosphate 119684-05-8, Mesoglycan
```

L16 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1998:689255 HCAPLUS

DOCUMENT NUMBER:

129:281053

TITLE:

INVENTOR(S):

Wound dressings containing active substances Woessner, Werner; Oswald, Ute; Meister, Frank; Hueckel, Marion; Mueller, Peter-Juergen; Buehler,

Konrad; Taplick, Thomas

PATENT ASSIGNEE(S):

Thueringisches Institut fuer Textil- und

Kunststoff-Forschung e.V., Germany; Hans Knoell Institut fuer Naturstoff-Forschung e.V.; GWE

Gesellschaft fuer Wissenschaft und Entwicklung m.b.H.;

Gothaplast Verbandpflasterfabrik G.m.b.H.

SOURCE:

Ger. Offen., 6 pp. CODEN: GWXXBX

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|------------------|----------|
| | | | | |
| DE 19712699 | A1 | 19981001 | DE 1997-19712699 | 19970326 |
| DE 19712699 | C2 | 20000525 | | |

DE 19712699 A wound plaster consists of an adhesive-coated backing layer, an overlay AB comprising a dried polysaccharide gel contg. medicinally active substances and excipients, and a removable release liner. The polysaccharide gel is dried by microwave irradn., optionally with the aid of heated gases and/or IR irradn.; this method provides homogeneous drying, without degrdn. of the active agents, to a film which does not have the spongy, mech. weak structure of freeze-dried polysaccharide films. Thus, a mixt. of hyaluronic acid (mol. wt. 1.5 .times. 106) 2, glycerin 2, p-hydroxybenzoic acid 0.06, and distd. water 95.94 parts was continuously applied to the Teflon-coated belt of a film-casting machine and passed through a 6 m-long, 25-kW microwave tunnel at 35 m/h with a countercurrent stream of air at 40-50.degree. to produce a film 240 .mu.m thick. This plasticized hyaluronic acid film was scraped off and layered onto a band of cotton fabric (180 g/m2) at 50.degree.; the fabric band was then placed in the middle of a strip of adhesive-coated backing material and covered with detachable polypropylene film.

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- L16 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
- IC ICM A61L015-28
 - ICS A61F013-02; A61L015-44; A61F017-00; A61K038-17; C08L005-00
- CC 63-7 (Pharmaceuticals)
- ST wound adhesive dressing polysaccharide gel; hyaluronate gel drug medical dressing
- IT Medical goods
 - (absorbents; wound dressings contg. active substances)
- IT Lipids, biological studies
 - Proteins (specific proteins and subclasses)
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (complexes, with hyaluronic acid; wound dressings contg. active substances)
- IT IR radiation

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Microwave
        (drying with; wound dressings contg. active substances)
     Polysaccharides, biological studies
TΤ
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (gels; wound dressings contg. active substances)
IT
    Gases
        (heated, drying with; wound dressings contg. active substances)
ΙT
    Absorbents
        (medical; wound dressings contg. active substances)
    Peptide complexes
TΨ
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (with hyaluronic acid; wound dressings contg. active substances)
IT
    Anti-inflammatory drugs
    Antioxidants
    Binders
    Blister
    Cotton fabrics
     Disinfectants
     Dressings (medical)
     Drugs
     Drying
     Emulsifying agents
     Fabrics
     Hydrocolloids
     Hydrogels
    Liposomes (drug delivery systems)
     Permeation enhancers
     Plasticizers
     Preservatives
     Thickening agents
        (wound dressings contg. active substances)
ΙT
    Lymphokines
     Vitamins
    RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (wound dressings contg. active substances)
    Glycosaminoglycans, biological studies
IT
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (wound dressings contg. active substances)
     50-81-7, L-Ascorbic acid, biological studies
ΙT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (antioxidant; wound dressings contg. active substances)
     55-56-1D, Chlorhexidine, compds. with glucose
ΙT
                                                      1837-57-6, Ethacridine
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (disinfectant; wound dressings contg. active substances)
TΤ
     260-94-6D, Acridine, derivs.
                                    65431-33-6D, Trypaflavine, derivs.
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (dyes; wound dressings contg. active substances)
IT
     56-81-5, 1,2,3-Propanetriol, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (plasticizer; wound dressings contg. active substances)
ΙT
     110-44-1, Sorbic acid
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (preservative; wound dressings contq. active substances)
ΙT
     99-96-7D, esters
```

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preservatives; wound dressings contg. active substances) ΙT 50-99-7D, D-Glucose, compds. with chlorhexidine 79-83-4, Pantothenic RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (wound dressings contg. active substances) ΙT 62-49-7D, Choline, complexes with hyaluronic acid 1398-61-4, Chitin 9000-01-5, Gum arabic 9000-07-1, Carrageenan 9000-30-0, Guar gum 9000-40-2, Locust bean gum 9000-65-1, Gum tragacanth 9000-69-5, F 9002-18-0, Agar 9004-32-4 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9004-61-9D, Hyaluronic acid, derivs. 9000-69-5, Pectin 9004-61-9D, Hyaluronic acid, esters 9005-25-8, Starch, biological 9005-32-7, Alginic acid 9005-49-6, Heparin, 9007-27-6, Chondroitin 9012-76-4, Chitosan biological studies 9050-67-3, Schizophyllan 9057-02-7, Pullulan 9067-32-7, Sodium hyaluronate 11138-66-2, Xanthan gum 39300-88-4, Tara gum 54724-00-4, 69992-87-6, Keratan 71010-52-1, Gellan gum Curdlan 73613-05-5, Fenugreek gum 75634-40-1, Dermatan 96949-21-2, Rhamsan gum 96949-22-3, Welan gum 111744-92-4, Benzyl hyaluronate 111745-19-8, Ethyl hyaluronate RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (wound dressings contg. active substances)

L16 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1996:725353 HCAPLUS

DOCUMENT NUMBER: 126:51022

TITLE: Gel-forming system for use as wound dressings

INVENTOR(S): Fox, Adrian S.; Allen, Amy E.

PATENT ASSIGNEE(S): Nepera, Inc., USA

SOURCE: U.S., 8 pp. CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
US 5578661 A 19961126 US 1994-221159 19940331

AB A gel-forming system comprising an aq. mixt. of a first component of at least one water-sol. polymer in an amt. sufficient to increase the initial viscosity of the mixt. and impart adhesion properties thereto; a second component of an acid-contg. polymer; a third component of an amino-contg. polymer; and water. This system has a pH 5.5-8.5 and the second and third components are each present in sufficient amts. which, in combination, increase the cohesiveness of the mixt. over time, such that the mixt. can be initially combined in a relatively fluid state and subsequently forms a cohesive gel structure. This system is useful as a wound dressing for deep wound cavities because the gel protects the wound and permits healing, does not interfere with new tissue growth or development, is capable of absorbing significant amts. of wound exudate, and has sufficient cohesive strength for subsequent removal from the cavity as an integral plug without interrupting the healing process. For example, a gel-forming compn. contained ethylene-maleic anhydride copolymer 0.5, N,O-carboxymethyl chitosan 2.5, PVP 10, polyethylene oxide 0.5, and NaOH 0.16 %.

=> d hitstr 3

L16 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS

IT 9003-01-4, Polyacrylic acid 9005-49-6, Heparin

, biological studies 25104-18-1, Poly(L-lysine)

25322-68-3, Polyethylene oxide 38000-06-5,

Poly(L-lysine)

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(gel-forming system for use as wound dressings)

RN 9003-01-4 HCAPLUS

CN 2-Propenoic acid, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 79-10-7 CMF C3 H4 O2

RN 9005-49-6 HCAPLUS

CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 25104-18-1 HCAPLUS

CN L-Lysine, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 56-87-1

CMF C6 H14 N2 O2

CDES 5:L

Absolute stereochemistry.

RN 25322-68-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$HO \longrightarrow CH_2 - CH_2 - O \longrightarrow n$$

RN 38000-06-5 HCAPLUS

CN Poly[imino[(1S)-1-(4-aminobutyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)

=> d ind 3

ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS. ICM C08L005-00 ICS C08L039-06; C08L071-02 NCL 524027000 CC 63-7 (Pharmaceuticals) ST wound dressing gel polymer mixt ΙT Dressings (medical) Electrolytes (gel-forming system for use as wound dressings) IT Glycosaminoglycans, biological studies Peptides, biological studies Platelet-derived growth factors Polysaccharides, biological studies Transforming growth factor .beta.1 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (gel-forming system for use as wound dressings) ΙT 526-95-4D, Gluconic acid, derivs. 9000-07-1, Carrageenan 9002-18-0, 9003-39-8, PVP Agar 9003-01-4, Polyacrylic acid 9004-61-9, Hyaluronic acid 9005-32-7, Alginic acid 9005-49-6, 9006-26-2, Ethylene-maleic anhydride Heparin, biological studies 9011-16-9, Maleic anhydride-methyl vinyl ether copolymer copolymer 9012-76-4, Chitosan **25104-18-1**, Poly(L-lysine) 28062-44-4, Acrylic 25322-68-3, Polyethylene oxide acid-vinylpyrrolidone copolymer 38000-06-5, Poly(L-lysine) 62229-50-9, Epidermal growth factor 83512-85-0, N-Carboxymethylchitosan 107043-88-9, N,O-Carboxymethylchitosan RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (gel-forming system for use as wound dressings) IT 56-81-5, Glycerol, biological studies 96-48-0, .gamma.-Butyryl lactone 97-64-3, Ethyl lactate 123-42-2, Diacetone alcohol 872-50-4, N-Methylpyrrolidone, biological studies 2687-91-4, N-Ethylpyrrolidone RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (humectant; gel-forming system for use as wound dressings)

L16 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1996:369827 HCAPLUS

DOCUMENT NUMBER: 125:35743

TITLE: Modified alginate fibers for wound dressings with

improved absorbancy

INVENTOR(S): Qin, Yimin; Gilding, Keith Dennis
PATENT ASSIGNEE(S): Innovative Technologies Limited, UK

SOURCE: PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English .

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. KIN | | | | ND | D DATE APPLICATION NO. DATE | | | | | | | | | | | | |
|-------|------------------------|------|-----|-----|-----|-----------------------------|------|------|--------------------------|------|-------------------|------|------|-----|------|------|-----|-----|
| | WO | 9610 | 106 | | A | 1 | 1996 | 0404 | | W | 0 19 | 95-G | B228 | 4 | 1995 | 0926 | | |
| • | | W: | AM, | AT, | AU, | BB, | BG, | BR, | BY, | CA, | CH, | CN, | CZ, | DE, | DK, | EE, | ES, | FI, |
| | | | GB, | GE, | HU, | IS, | JP, | KΕ, | KG, | ΚP, | KR, | ΚZ, | LK, | LR, | LT, | LU, | LV, | MD, |
| | | | MG, | MK, | MN, | MW, | MX, | NO, | NZ, | PL, | PT, | RO, | RU, | SD, | SE, | SG, | SI, | SK, |
| | | | ТJ, | TM | | | | | | | | | | | | | | |
| | | RW: | ΚE, | MW, | SD, | SZ, | ŪG, | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙE, | IT, |
| | | | LU, | MC, | ΝL, | PT, | SE, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | ML, | MR, | NE, |
| | | | SN, | TD, | TG | | | | | | | | | | | | | |
| | AU 9535306 A1 1996041 | | | | | | | | | | | | | | 1995 | 0926 | | |
| | | 2307 | | | | | | | | G! | в 19 [.] | 97-6 | 596 | | 1995 | 0926 | | |
| | | 2307 | | | | | | | | | | | | | | | | |
| | EΡ | 7836 | | | | | | | | | | | 3212 | 7 | 1995 | 0926 | | |
| | | | | DE, | | | | | | | | | | | | | | |
| | | 1050 | | | | | | | | | | | | | 1995 | 0926 | | |
| | US 6080420 A 2000062 | | | | | | | | | | | | | | | | | |
| PRIOR | PRIORITY APPLN. INFO.: | | | | | | | | GB 1994-19572 A 19940929 | | | | | | | | | |
| | | | | | | | | | (| GB 1 | 995- | 1514 | | Α | 1995 | 0126 | | |
| | | | | | | | | | (| GB 1 | 995- | 1693 | 0 | A | 1995 | 0818 | | |
| | | | | | | | | | | WO 1 | 995-0 | GB22 | 84 | W | 1995 | 0926 | | |

AB The title fibers are prepd. by spinning aq. solns. contg. 70-95:5-30 (wt. ratio) mixts. of alginates and water-sol. nonalginate polymers [e.g., polysaccharides, poly(carboxyamino acids), poly(acrylic acid), poly(methacrylic acid) or salts thereof] into a coagulating bath. An aq. dope contg. Na alginate (Protanal LF 10/62) 12, CM-cellulose 1.5, and high-methyloxy pectin 1.5 kg was spun at 12 m/min, taken up at 7.2 m/min, drawn 80.degree., washed, dried, crimped, and cut to give staple fibers suitable for nonwoven wound dressings.

L16 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1995:324872 HCAPLUS

DOCUMENT NUMBER: 122:89477

TITLE: Hydrolytically labile cyanogen halide-crosslinked

polysaccharide microspheres

INVENTOR(S): Smith, Daniel J.; Chakravarthy, Debashish

PATENT ASSIGNEE(S): University of Akron, USA SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
WO 9427647 A1 19941208 WO 1994-US5702 19940519

W: CA, JP

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE US 5549908 A 19960827 US 1993-65742 19930520 PRIORITY APPLN. INFO.: US 1993-65742 19930520

PRIORITY APPLN. INFO.:

US 1993-65742 19930520

AB Water swellable and hydrolytically labile (and therefore potentially biodegradable) non-toxic microspheres or beads comprise a polysaccharide (e.g. dextran) crosslinked with a cyanogen halide (e.g. cyanogen bromide) in an aq. alk. medium which is a disperse phase of a water-in-oil dispersion. The microspheres are useful in the treatment of wounds, in particular as an absorptive agent for wound exudates. The microspheres may be formed into a wound dressing which includes a blend of the microspheres and a hydrophobic adhesive matrix material on a waterproof backing sheet.

=> d hitstr ind 5

L16 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS

IT 9042-14-2P, Dextran sulfate

RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (crosslinked; swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

RN 9042-14-2 HCAPLUS

CN Dextran, hydrogen sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 9004-54-0 CMF Unspecified CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 7664-93-9 CMF H2 O4 S

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IC ICM A61L015-00

CC 63-6 (Pharmaceuticals)

ST cyanogen halide crosslinking polysaccharide microsphere bead; wound dressing crosslinking polysaccharide microsphere bead

IT Crosslinking agents

(cyanogen halides; swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

IT Pharmaceutical dosage forms

(beads, swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

IT Medical goods

(dressings, swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

IT Pharmaceutical dosage forms

(microspheres, swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

IT 74-79-3DP, Arginine, grafts with dextran 9004-54-0P, Dextran, biological studies 9042-14-2P, Dextran sulfate

RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (crosslinked; swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

IT 506-68-3, Cyanogen bromide

RL: RCT (Reactant)

(crosslinking agent; swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

=> d ibib abs 6

L16 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1994:563976 HCAPLUS

DOCUMENT NUMBER: 121:163976

TITLE: Heparin-fibroblast growth factor-fibrin

complex: in vitro and in vivo applications to

collagen-based materials

AUTHOR(S): DeBlois, Chantal; Cote, Marie-France; Doillon, J.

CORPORATE SOURCE: Laval University, Quebec, PQ, G1L 3L5, Can.

SOURCE: Biomaterials (1994), 15(9), 665-72

CODEN: BIMADU; ISSN: 0142-9612

DOCUMENT TYPE: Journal LANGUAGE: English

Biol. mols. such as fibrin and growth factors could have interesting features to design bioactive biomaterials and particularly collagen-based materials used as connective tissue replacement. Different combinations of fibroblast growth factor (FGF) and heparin complexes to fibrin were analyzed. In vitro, FGF bound to matrix was rapidly, but partially released, specifically with heparin. Heparin concns. were progressively equilibrated between matrix and medium. DNA replication of fibroblasts grown either on or within fibrin matrixes was increased in the presence of both FGF and high doses of heparin incorporated in fibrin. S.c. implantations of collagen sponges impregnated with composite fibrin matrixes showed qual. and quant. tissue ingrowth within the sponges. The noncrosslinked collagen of fibrin-impregnated sponges swelled after implantation. The resulting fibroblast-infiltrated tissue resembled a normal dense connective tissue that was obsd. particularly in the presence of high doses of heparin and FGF incorporated in fibrin.

=> d ibib abs hitstr

L23 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1994:638475 HCAPLUS

DOCUMENT NUMBER:

121:238475

TITLE:

.....

Supplemented and unsupplemented tissue sealants,

methods of their production and use

INVENTOR(S):

Nunez, Hernan A.; Drohan, William Nash; Burgess, Wilson Hales; Greisler, Howard P.; Hollinger, Jeffrey

O.; Lasa, Carlos I., Jr.; Maciag, Thomas; Macphee,

Martin James

PATENT ASSIGNEE(S):

American National Red Cross, USA; Loyola University of

Chicago; United States Dept. of the Army

SOURCE:

PCT Int. Appl., 140 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PA' | PATENT NO. KIN | | | DATE | | APPLICATION NO |). | DATE | | | | |
|---------|-------------------|------|--------|-----------|-----|-----------------|-----|----------|-----|-----|----|--|
| WO | 9420133 W: AU, | | | 19940915 | | WO 1994-US2708 | 3 | 19940314 | | | | |
| | • | • | | , DK, ES, | FR, | GB, GR, IE, IT, | LU, | MC, NL, | PT, | SE | | |
| CA | 2158134 | | AA | 19940915 | | CA 1994-215813 | 34 | 19940314 | | | | |
| AU | 9463648 | | A1 | 19940926 | | AU 1994-63648 | | 19940314 | | | | |
| AU | 696691 | | B2 | 19980917 | | | | | | | | |
| EP | 696201 | | A1 | 19960214 | | EP 1994-910927 | 7 | 19940314 | | | | |
| | R: AT, | BE, | CH, DE | , DK, ES, | FR, | GB, GR, IE, IT, | LI | LU, MC, | NL, | PT, | SE | |
| JP | 09502161 | | Т2 | 19970304 | | JP 1994-520353 | 3 | 19940314 | | | | |
| AU | 9884192 | | A1 | 19981105 | | AU 1998-84192 | | 19980911 | | | | |
| AU | 733471 | | B2 | 20010517 | | | | | | | | |
| PRIORIT | Y APPLN. 1 | NFO. | . : | | | US 1993-31164 | Α | 19930312 | | | | |
| | | | | | | AU 1994-63648 | АЗ | 19940314 | | | | |
| | | | | | | WO 1994-US2708 | W | 19940314 | | | | |

AB This invention provides supplemented and unsupplemented tissue sealants (TSs), such as fibrin glue, as well as methods of their prodn. and use. In one embodiment, this invention provides TSs that do not inhibit full thickness skin wound healing. This invention also provides growth factor(s) - and/or drug(s) - supplemented TSs and methods of their prodn. and use. In one embodiment, the TS is supplemented with a growth factor(s) and can be used to promote (1) wound healing, such as that of skin or bone, (2) endothelialization of vascular prostheses, (3) the proliferation and/or differentiation of animal cells, and/or (4) the directed migration of animal cells. Exemplified embodiments include fibrin glue that is supplemented with fibroblast growth factors and/or bone morphogenetic proteins and polytetrafluorethylene vascular grafts pressure perfused with fibrin glue contq. heparin-binding growth factor-1. In another embodiment the supplemented TS is used to produce a localized delivery of a growth factor(s) and/or a drug(s), such as 5-fluorouracil and tetracycline.

=> d ibib abs hitstr 2

L23 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1993:198118 HCAPLUS

DOCUMENT NUMBER:

118:198118

TITLE:

Development of hydrogel-containing stabilized basic

fibroblast growth factor for wound treatment

AUTHOR(S):

Tefft, J.; Roskos, K. V.; Heller, J.

CORPORATE SOURCE:

Controlled Release Biomed. Polym. Dep., SRI Int.,

Menlo Park, CA, 94025, USA

SOURCE:

Proc. Int. Symp. Controlled Release Bioact. Mater., 19th (1992), 371-2. Editor(s): Kopecek, Jindrich.

Controlled Release Soc.: Deerfield, Ill.

CODEN: 58JTAJ

DOCUMENT TYPE:

Conference

LANGUAGE:

English
The proposed hydrogel wound **dressing** consists of a collagenheparin matrix integrated into a starch support. This hydrogel

also contains a stabilizing heparin-basic fibroblast

growth factor (bFGF) complex where the bFGF remains immobilized within the polymer network until delivery. This hydrogel mimics the manner in which bFGF is stored in an insol. substrate such as the extracellular matrix.

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L23 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS

CC 63-7 (Pharmaceuticals)

ST hydrogel fibroblast growth factor wound dressing

IT Medical goods

(dressings, hydrogels, basic fibroblast growth factor-contg., for wound treatment)

IT 106096-93-9, Basic fibroblast growth factor

RL: BIOL (Biological study)

(dressing hydrogels contg., for wound treatment)

=> d ibib abs hitstr 3

L23 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1988:124468 HCAPLUS

DOCUMENT NUMBER:

108:124468

TITLE:

The influence of heparin on the wound healing response

to collagen implants in vivo

AUTHOR(S):

McPherson, John M.; Ledger, Philip W.; Ksander, George; Sawamura, Steven J.; Conti, Annemarie;

Kincaid, Steven; Michaeli, Dov; Clark, Richard A. F.

CORPORATE SOURCE:

Connect. Tissue Res. Lab., Collagen Corp., Palo Alto,

CA, 94303, USA

SOURCE:

Collagen Relat. Res. (1988), 8(1), 83-100 CODEN: CREXDV; ISSN: 0174-173X

DOCUMENT TYPE:

Journal English

LANGUAGE: The biol. response to fibrillar collagen (collagen) and fibrillar collagen plus heparin (collagen/heparin) implants were compared in the rat s.c. and guinea pig dermal wound models. The reconstituted bovine dermal collagen implants were injected s.c. in rats at concns. ranging from 18 to 30~mg/mL and in vols. ranging from 0.5 to 1.0 mL. The biol. response to the collagen implants alone was characterized by a transient invasion of a modest no. of inflammatory cells within the first 3 days of implantation that was followed by limited fibroblast invasion into the peripheral 1/3 of the implant during the course of the next 3 to 4 wk. Occasionally, blood vessels were obsd. to invade the peripheral regions of the implant. The degree (no.) and extent (depth) of cell invasion were inversely related to initial collagen implant concn. Addn. of heparin (0.3-20 .mu.g/mg collagen) to these implants resulted in a significant dose-dependent increase in the degree and extent of fibroblast invasion. Radiolabeling studies showed that the collagen and collagen/heparin implants were cleared from the subcutis at identical rates. Implantation of these formulations in a guinea pig dermal wound model was also performed, using a semi-occlusive wound dressing (Opsite) to maintain the implant in the wound site. The fibrillar collagen implant alone was pushed upward by developing granulation tissue at the base of the wound and served as a support for epidermal cell migration, proliferation, and differentiation as wound closure proceeded. The implant was slowly invaded and turned over as granulation tissue developed from the base and margins of the wound bed. The inclusion of heparin in these implants resulted in a significantly different pattern of wound healing. The collagen/ heparin implants histol. presented a more broken-up or porous appearance following implantation, which was assocd. with a greater degree of penetration of developing granulation tissue into the implant itself as compared to the collagen implants. Radiolabeling studies revealed that clearance rates of implants with and without heparin from wound sites were similar, as noted in the rat subcutis. Laser doppler flowmetry studies suggested that the heparin-contg. implants were more vascular than control wound sites or sites treated with collagen alone.

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L36 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2002:84615 HCAPLUS

DOCUMENT NUMBER: 136:139888

TITLE: Amphipathic coating for modulating cellular adhesion

composition

INVENTOR(S): Zamora, Paul O.; Osaki, Shigemasa; Tsang, Ray PATENT ASSIGNEE(S): Biosurface Engineering Technologies, Inc., USA

SOURCE: U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 399,119,

abandoned. CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PAT | PATENT NO. | | | KI | ND | DATE | | | A | PPLI | CATI | ON N | 0. | DATE | | | |
|----------|----------------------|-------------------|-------------------|-------------------|-------------------|----------------------|-------------------|-------------------|----------------------|----------------------|-------------------------|-------------------|-------------------|--------------------------------------|----------------------|-------------------|-------------------|
| US | 6342 5955 1159 | 588 | | B A A | | 2002 1999 2001 | 0921 | | U | S 19 | 00-6: 98-1: 99-9: | 5927 | 6 | 2000 1998 1999 | 0922 | | |
| | R: | DE, | ES, | FR, | GB, | IT, | ΙE | | | | | | _ | 2001 | | | |
| | W: | CO, HR, LT, | CR, HU, LU, | CU, ID, LV, | CZ, IL, MA, | DE, IN, MD, | DK, IS, MG, | DM, JP, MK, | DZ, KE, MN, | EE, KG, MW, | ES, KP, MX, | FI, KR, MZ, | GB, KZ, NO, | BZ, GD, LC, NZ, UA, | GE, LK, PL, | GH, LR, PT, | GM, LS, RO, |
| | RW: | GH, DE, | GM, DK, | KE, ES, CG, | LS, FI, CI, | FR, CM, | MZ, GB, GA, | SD, GR, GN, | SL, IE, GQ, | SZ, IT, GW, | TZ, LU, ML, | UG, MC, MR, | ZW, NL, NE, | AT, PT, SN, | SE, TD, | TR, | • |
| PRIORITY | APP | LN. | INFO | .: | | | | 1 | US 1 US 1 WO 1 | 999- 997- 999- | 3991 6837 US45 | 19 4P 0 | B2 P W | 1998 1999 1997 1999 2000 | 0920 1222 0108 | | |

The present invention provides an anti-thrombogenic and cellular-adhesion coating compn. for blood-contacting surfaces. The coating comprises a covalent complex of 1-30 hydrophobic silyl moieties, directly bound to a heparin mol. via covalent bonding, with an adhesive mol. directly bound to the heparin mol. In one embodiment, the coating comprises benzyl-(1,2-dimethyl)disilylheparin, wherein an adhesive mol., such as fibronectin, is bound to the heparin. Benzylmagnesium chloride was treated serially with chloro(chloromethyl)dimethylsilane to give a benzyl-(1,2dimethyl)disilyl compd. This compd. was modified to form an activated succinimidyl ester that was, in turn, conjugated to heparin to form a benzyl-(1,2-dimethyl)disilylheparin. The silylheparin coating may be applied to any polymeric substrate, either forming a medical or other implantable device, or coated or otherwise forming a surface of a medical or other implantable device.

forming a surface of a medical or other implantable device.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAI

THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d kwic

L36 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AB . . coating compn. for blood-contacting surfaces. The coating

```
comprises a covalent complex of 1-30 hydrophobic silyl moieties, directly
bound to a heparin mol. via covalent bonding, with an adhesive
mol. directly bound to the heparin mol. In one embodiment, the
coating comprises benzyl-(1,2-dimethyl)disilylheparin, wherein an adhesive
mol., such as fibronectin, is bound to the heparin.
Benzylmagnesium chloride was treated serially with
chloro(chloromethyl)dimethylsilane to give a benzyl-(1,2dimethyl)disilyl
compd. This compd. was modified to form an activated succinimidyl ester
that was, in turn, conjugated to heparin to form a
benzyl-(1,2-dimethyl)disilylheparin. The silyl-heparin coating
may be applied to any polymeric substrate, either forming a medical or
other implantable device, or coated or otherwise.
amphipathic coating cellular adhesion medical device; heparin
coating medical device benzyldimethysilylmethyl prepn
Animal cell
Cell adhesion
Coating materials
  Fibroblast
Medical goods
Nerve
Prosthetic materials and Prosthetics
T cell (lymphocyte)
   (amphipathic coating for modulating cellular adhesion compn.)
9005-49-6DP, Heparin, reaction products with
benzylbis(dimethysilylmethyl) deriv. 392298-24-7DP, reaction products
with heparin
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)
   (amphipathic coating for modulating cellular adhesion compn.)
9002-72-6, Growth hormone
                          9005-49-6, Heparin, biological
studies
          9042-14-2, Dextran sulfate
                                       24937-49-3,
Polyornithine
                25104-12-5, Polyornithine
                                            25104-18-1, Polylysine
38000-06-5, Polylysine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
   (amphipathic coating for modulating cellular adhesion compn.)
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L36 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2000:175701 HCAPLUS

DOCUMENT NUMBER:

132:212734

TITLE:

Hydrogel compositions for the controlled release

administration of growth factors

INVENTOR(S):

Jennings, Robert N., Jr.; Yang, Bing; Protter, Andrew

A.; Wang, Yu-Chang John

PATENT ASSIGNEE(S):

Scios Inc., USA

SOURCE:

PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PA | PATENT NO. KIND DATE | | | | | | | | I | APPLI | CATI | и ис | 0. | DATE | | | |
|---------|----------------------|------|------|-----|-----|------|------|-----|------|--------|-------|------|-----|------|------|-----|-----|
| WC | 2000 | 0137 | 10 | A | 2 | 2000 | 0316 | | V | vo 19 | 99-U | S203 | 82 | 1999 | 0903 | | |
| | W: | ΑE, | AL, | AM, | AT, | AU, | AZ, | BA, | BB, | BG, | BR, | BY, | CA, | CH, | CN, | CU, | CZ, |
| | | DE, | DK, | EE, | ES, | FI, | GB, | GD, | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, |
| | * | JP, | ΚE, | KG, | ΚP, | KR, | ΚZ, | LC, | LK, | LR, | LS, | LT, | LU, | LV, | MD, | MG, | MK, |
| | | MN, | MW, | MX, | NO, | NZ, | PL, | PT, | RO, | RU, | SD, | SE, | SG, | SI, | SK, | SL, | ТJ, |
| | | TM, | TR, | TT, | UA, | UG, | US, | UZ, | VN, | YU, | ZA, | ZW, | AM, | ΑZ, | BY, | KG, | ΚZ, |
| | | MD, | RU, | ТJ, | TM | | | | | | | | | | | | |
| | RW: | GH, | GM, | ΚE, | LS, | MW, | SD, | SL, | SZ, | UG, | ZW, | AT, | BE, | CH, | CY, | DE, | DK, |
| | | ES, | FI, | FR, | GB, | GR, | ΙE, | ΙΤ, | LU, | MC, | NL, | PT, | SE, | BF, | ВJ, | CF, | CG, |
| | | CI, | CM, | GΑ, | GN, | GW, | ML, | MR, | NE, | SN, | TD, | TG | | | | | |
| AU | 9959 | 095 | | A | 1 | 2000 | 0327 | | I | AU 19 | 99-5 | 9095 | | 1999 | 0903 | | |
| ÉP | 1107 | 791 | | A | 2 | 2001 | 0620 | | E | EP 19 | 99-9 | 4675 | 9 | 1999 | 0903 | | |
| | R: | AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙΤ, | LI, | LU, | NL, | SE, | MC, | PT, |
| | | | | | | FI, | | | | | | | | | | | |
| US | 6331 | 309 | | В | 1 | 2001 | 1218 | | J | JS 19 | 99-3 | 9016 | 4 | 1999 | 0903 | | |
| PRIORIT | Y APP | LN. | INFO | .: | | | | | US 1 | L998- | 9916 | 3 P | Р | 1998 | 0904 | | |
| | | | | | | | | | US 1 | L998- | 9916 | 8 | P | 1998 | 0904 | | |
| | | | | | | | | 1 | WO 1 | L999-1 | US20: | 382 | W | 1999 | 0903 | | |

AB Compns. and methods are disclosed for the controlled release delivery of polypeptide growth factors. The compns. of the invention are hydrogels which comprise: a polypeptide growth factor having at least one region of pos. charge; a physiol. acceptable water-miscible anionic polymer; a physiol. acceptable nonionic polymeric viscosity controlling agent; and water. An example compn. contained basic fibroblast growth factor, 10% polyoxyethylene-polyoxypropylene block copolymer and Na CM-cellulose.

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L36 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1998:709125 HCAPLUS

DOCUMENT NUMBER:

129:332221

TITLE:

Multifunctional polymeric tissue coatings, their

preparation and use as protective coating or

encapsulant

INVENTOR(S):

Hubbell, Jeffrey A.; Elbert, Donald L.; Herbert,

Curtis B.

PATENT ASSIGNEE(S):

California Institute of Technology, USA

SOURCE:

PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PAT | PATENT NO. | | | | ND | DATE | | | A | PPLI | CATI | ои ис | ο. | DATE | | | |
|-------|------------|---------|-------|-------|-------|------|------|-----|------|------|------|-------|-----|------|------|-----|-----|
| WO | 98479 | 948 | | А | 1 | 1998 | 1029 | | W | 0 19 | 98-U | 57590 | 0 | 1998 | 0417 | | k. |
| | W: | AL, | ΑU, | BA, | BB, | BG, | BR, | CA, | CN, | CU, | CZ, | EE, | GE, | GW, | HU, | ID, | IL, |
| | | IS, | JP, | KP, | KR, | LC, | LK, | LR, | LT, | MG, | MK, | MN, | MX, | NO, | NZ, | PL, | RO, |
| | | SG, | SI, | SK, | SL, | TR, | TT, | UA, | US, | UZ, | VN, | YU, | AM, | AZ, | BY, | KG, | KZ, |
| | | MD, | RU, | ТJ, | ΜT | | | | | | | | | | | | |
| | RW: | GH, | GM, | KE, | LS, | MW, | SD, | SZ, | UG, | ZW, | ΑT, | BE, | CH, | CY, | DE, | DK, | ES, |
| | | FI, | FR, | GB, | GR, | ΙE, | ΙΤ, | LU, | MC, | NL, | PT, | SE, | BF, | ВJ, | CF, | CG, | CI, |
| | | CM, | GA, | GN, | ML, | MR, | ΝE, | SN, | TD, | TG | | | | | | | |
| AU | 98712 | 211 | | Α | 1 | 1998 | 1113 | | ΑI | U 19 | 98-7 | 1211 | | 1998 | 0417 | | |
| EP | 97569 | 91 | | Α | 1 | 2000 | 0202 | | E | P 19 | 98-9 | 18250 | С | 1998 | 0417 | | |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | IT, | LI, | LU, | NL, | SE, | MC, | PT, |
| | | ΙE, | FI | | | | | | | | | | | | | | |
| ORITY | (APP | ĹN. | INFO. | . : | | | | | US 1 | 997- | 4472 | 6P | P | 1997 | 0418 | | |
| | | | | | | | | | | | | | | | | | |

PRI

WO 1998-US7590 W 19980417

AB Biocompatible compns. for coating biol. and nonbiol. surfaces (metal), minimize or prevent cell-cell contact and tissue adhesion. Polyethylene glycol/polylysine (PEG/PLL) block or comb-type copolymers with high mol. wt. PLL (>1000, more preferably >100,000); PEG/PLL copolymers in which the PLL is a dendrimer which is attached to 1 end of the PEG; and multilayer compns. including alternating layers of polycationic and polyanionic materials are prepd. for coating substrates. wts. are selected such that the PEG portion of the copolymer inhibits cellular interactions, and the PLL portion adheres well to tissues. The compns. inhibit formation of post-surgical adhesions, protect damaged blood vessels from thrombosis and restenosis, and decrease the extent of metastasis of attachment-dependent tumor cells. Polyethylene glycol-polylysine block graft copolymer was used to coat a polystyrene cell culture well showed resistance to cell spread when seeded with human foreskin fibroblast cells.

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- L36 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS
- ICM C08G081-00 IC ICS A61K009-50
- CC 42-10 (Coatings, Inks, and Related Products) Section cross-reference(s): 35, 63
- ST polyethylene glycol polylysine block graft coating;

```
dendritic polyethylene glycol polylysine coating;
     cationic polymer multilayer coating; anionic polymer multilayer coating;
     tissue protective coating comb polymer; cell adhesion resistance coating
ΙT
     Polysaccharides, uses
     RL: TEM (Technical or engineered material use); THU (Therapeutic use);
     BIOL (Biological study); USES (Uses)
        (cationic; in multilayer coatings of multifunctional polymeric tissue
        coatings)
ΙT
     Dendritic polymers
     RL: PRP (Properties); TEM (Technical or engineered material use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (ethylene oxide-lysine copolymer; multifunctional polymeric tissue
        coatings)
ΙT
     Peptides, uses
     RL: TEM (Technical or engineered material use); THU (Therapeutic use);
     BIOL (Biological study); USES (Uses)
        (in multilayer coatings of multifunctional polymeric tissue coatings)
    Medical goods
IT
        (multilayer coatings and multifunctional polymeric tissue coatings for
        application to)
    Animal tissue
TΤ
     Blood vessel
        (multilayer coatings and multifunctional polymeric tissue coatings for
        protection of)
IT
     Tumors (animal)
        (multilayer coatings and multifunctional polymeric tissue coatings for
        resistance to attachment of)
ΙT
    Block polymers
    Graft polymers
    RL: TEM (Technical or engineered material use); THU (Therapeutic use);
    BIOL (Biological study); USES (Uses)
        (of polycationic unit and non-tissue binding unit; multifunctional
        polymeric tissue coatings)
ΙT
     Polyamides, uses
    RL: TEM (Technical or engineered material use); THU (Therapeutic use);
    BIOL (Biological study); USES (Uses)
        (poly(amino acids); in multilayer coatings of multifunctional polymeric
        tissue coatings)
TΤ
    Quaternary ammonium compounds, uses
    RL: TEM (Technical or engineered material use); THU (Therapeutic use);
    BIOL (Biological study); USES (Uses)
        (polymers; in multilayer coatings of multifunctional polymeric tissue
        coatings)
ΙT
    110067-85-1, Ethylene oxide-lysine copolymer
    RL: PRP (Properties); TEM (Technical or engineered material use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (dendritic; multifunctional polymeric tissue coatings)
                              9000-21-9, Furcellaran
TΤ
    9000-07-1, Carrageenan
                                                       9000-69-5, Pectin
    9002-98-6
                 9003-01-4, Polyacrylic acid
                                               9004-32-4, Sodium carboxymethyl
                 9004-34-6D, Cellulose, oxidized
    cellulose
                                                   9004-61-9, Hyaluronic acid
    9005-32-7D, Alginic acid, salts
                                       9005-49-6, Heparin, uses
                                      9042-14-2, Dextran
    9007-28-7, Chondroitin sulfate
              9050-30-0, Heparan sulfate
                                            9060-90-6,
    sulfate
    Poly(aminostyrene)
                          11138-66-2, Xanthan
                                                24937-47-1, Poly(arginine)
    24937-49-3, Poly(ornithine)
                                   24967-94-0, Dermatan sulfate
                                                                   25087-26-7,
    Polymethacrylic acid
                            25104-12-5, Poly(ornithine)
                                                          25212-18-4,
                      26062-48-6, Poly(histidine)
    Poly(arginine)
                                                    26853-89-4, Poly(D-lysine)
    26854-81-9, Poly(histidine)
                                   26913-90-6, Poly(D-lysine)
                                                                 69577-67-9D.
    Poly(2-aminoacrylic acid), esters
                                         215295-50-4
                                                       215295-53-7
    215295-55-9
                   215295-58-2
                                215295-61-7
                                               215295-64-0
                                                             215295-67-3
```

=> d ibib abs hitstr 4

L36 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS 1997:245943 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 126:313828

TITLE: Characterization of a 50-kDa component of epithelial

basement membranes using GDA-J/F3 monoclonal antibody

AUTHOR(S): Gayraud, Barbara; Hopfner, Bianca; Jassim, Ali;

Aumailley, Monique; Bruckner-Tuderman, Leena

CORPORATE SOURCE: Institut de Biologie et Chimie des Proteines, CNRS,

Lyon, 69367, Fr.

J. Biol. Chem. (1997), 272(14), 9531-9538 CODEN: JBCHA3; ISSN: 0021-9258 SOURCE:

PUBLISHER: American Society for Biochemistry and Molecular

Biology

DOCUMENT TYPE: Journal LANGUAGE: English

AΒ Using the monoclonal antibody GDA-J/F3, a 50-kDa noncollagenous component of human skin basement membrane zone was identified. Immunofluorescence stainings of normal human skin with the GDA-J/F3 antibody showed a linear fluorescence decorating the basement membrane zone. With immunoelectron microscopy, the epitope was localized to the insertion points of the anchoring fibrils into the lamina densa. The antigen is distinct from collagen VII, from the main structural protein of the anchoring fibrils, and from several other structural mols. of the basement membrane zone, because the GDA-J/F3 antibody did not react with purified basement membrane components in vitro. In serum-free cultures, the antigen was synthesized and secreted by normal and transformed human keratinocytes and to a lesser extent by normal human skin fibroblasts. Immunopptn. of radiolabeled epithelial cell-conditioned medium with the GDA-J/F3 antibody yielded two polypeptides that migrated on SDS-PAGE with apparent mol. masses of 46 and 50 kDa under nonreducing conditions. Using reducing gels, only the 50-kDa polypeptide was obsd. The antigen was resistant to digestion with bacterial collagenase but sensitive to trypsin and pepsin. It also bound to heparin and DEAE cellulose at low ionic strength and alk. pH. These findings indicate that the GDA-J/F3 antigen is a small globular disulfide-bonded protein with a potential to interact with basement membrane proteoglycans. Integration of the GDA-J/F3 antigen into the histoarchitecture of the dermo-epidermal junction is dependent on the presence of collagen VII, because the GDA-J/F3 epitope was missing in several patients with a genetic blistering disorder of the skin, epidermolysis bullosa dystrophica, who lacked collagen VII and anchoring fibrils.

=> d ibib abs hitstr 5

L36 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1990:11911 HCAPLUS

DOCUMENT NUMBER: 112:11911

TITLE: Gel formulation containing

polypeptide growth factors

INVENTOR(S): Finkenaur, Amy L.; Cohen, Jonathan M.; Shalaby, Shalaby W.; Sandoval, Elisabeth A.; Bezwada, Rao S.;

Kronenthal, Richard L.

PATENT ASSIGNEE(S): Ethicon, Inc., USA

SOURCE: Eur. Pat. Appl., 16 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATÉ |
|----------------------|--------|--------------|-----------------------|----------|
| | | | | |
| EP 312208 | A1 | 19890419 | EP 1988-308574 | 19880916 |
| R: AT, BE, | CH, DE | , ES, FR, GI | B, IT, LI, LU, NL, SE | |
| AU 8822235 | A1 | 19890323 | AU 1988-22235 | 19880914 |
| JP 02000112 | A2 | 19900105 | JP 1988-232102 | 19880916 |
| ZA 8806947 | Α | 19900530 | ZA 1988-6947 | 19880916 |
| PRIORITY APPLN. INFO | .: | | US 1987-98816 A | 19870918 |
| | | | US 1988-233483 A | 19880819 |

AB Gel formulations contain polypeptide growth factors having human mitogenic or angiogenic activity and water sol. polymers for providing viscosities within various ranges detd. by the application of the gels. These gel formulations are useful for topical or incisional wound healing fur cutaneous wounds, in the anterior chamber of the eye and other ophthalmic wound healing. These formulations provide controlled release and increased contact time of the growth factor to the wound site. Thus, 6.3 g methylparaben, 0.7 g propylparaben, and 177.5 g mannitol was dissolved in 3500 mL water and to this soln. was added 17.5 g powd. poly(acrylic acid) (Carbopol 940) with mixing at 1000 rpm. The soln. was neutralized with 10% NaOH and 900 g resultant gel was removed and autoclaved, followed by addn. of 12 mL sterile EGF (1.18 mg/mL) to give a sterile gel (viscosity 490,000-520,000 cps) contg. 15.6 .mu.g EGF/mL. This gel gave an enhanced rate and quality of sound healing in pig and guinea pig partial thickness skin excision models.

=> d ibib abs hitstr 6

L36 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1983:450861 HCAPLUS

DOCUMENT NUMBER: 99:50861

TITLE: Serum spreading factor (vitronectin) is present at the

cell surface and in tissues

AUTHOR(S): Hayman, Edward G.; Pierschbacher, Michael D.; Ohgren,

Yvonne; Ruoslahti, Erkki

CORPORATE SOURCE: Cancer Res. Cent., La Jolla Cancer Res. Found., La

Jolla, CA, 92037, USA

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1983), 80(13), 4003-7

CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal LANGUAGE: English

Monoclonal antibodies were prepd. against a cell attachment-promoting protein, serum spreading factor, which had been partially purified from human serum by chromatog. on glass bead columns. The antibodies selected were those that reacted with polypeptides that had cell attachment-promoting activity after SDS polyacrylamide gel electrophoresis. Immunochromatog. of human plasma on columns contg. the monoclonal antibodies followed by affinity chromatog. on heparin -Sepharose yielded material that in SDS polyacrylamide gel electrophoretic anal. gave polypeptides of mol. mass 65 and 75 kilodaltons. Both polypeptides bound each of 3 monoclonal antibodies and had cell attachment-promoting activity after transfer to nitrocellulose Immunofluorescent staining of tissues with the monoclonal antibodies revealed a fibrillar pattern that was mostly assocd. with loose connective tissue and overlapped with fibronectin fibrils. Fetal membrane tissue, which showed strong staining with the antibodies in immunofluorescence, also gave 65- and 75-kilodalton polypeptides with cell attachment-promoting activity after chromatog. of columns contg. the monoclonal antibodies. One source of the tissue protein may be fibroblastic cells, because cultured human fibroblasts also stained with the monoclonal antibodies. The staining was fibrillar and appeared to be assocd. with the cell surface extracellular matrix. name vitronectin is proposed for the various forms of this protein, on the basis of its binding to glass and its adhesive properties.

L16 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1999:42596 HCAPLUS

DOCUMENT NUMBER: 130:115061

TITLE: Wound dressing comprising a biodegradable cell

anchoring layer

INVENTOR(S): Thomson, Brian Mark; Ali, Saad Abdul Majeed; Medcalf,

Nicholas; Maltman, John; Winter, Sharon Dawn

PATENT ASSIGNEE(S): Smith & Nephew Plc, UK SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PA' | PATENT NO. K | | | | | DATE APPLICATION NO. DA | | | | | DATE | | | | | | |
|----------|--------------|------|-------|-----|-----|-------------------------|------|-----|----|-------|------|-------|-----|------|------|-----|-----|
| | | | | | | | | | | | | | | | | | |
| WO | 9900 | 151 | | A: | 2 | 1999 | 0107 | | 1 | WO 19 | 98-G | B188: | 2 | 1998 | 0626 | | |
| WO | 9900 | 151 | | A. | 3 | 1999 | 0325 | | | | | | | | | | |
| | W: | AL, | AM, | ΑT, | AU, | AZ, | BA, | BB, | BG | , BR, | BY, | CA, | CH, | CN, | CU, | CZ, | DE, |
| | | DK, | EE, | ES, | FI, | GB, | GE, | GH, | GM | , GW, | HU, | ID, | IL, | IS, | JP, | KE, | KG, |
| | | - | • | | • | | | | | , LU, | | | | - | | | |
| | | NO. | NZ. | PL. | PT. | RO, | RU. | SD. | SE | , SG, | SI, | SK, | SL. | TJ. | TM. | TR. | TT, |
| | | | • | • | • | , | • | • | | , AZ, | • | • | • | • | • | • | • |
| | RW: | • | | | | | • | | | , ZW, | | | | | | | |
| | | • | • | • | • | • | • | | | , NL, | • | • | • | • | , | • | • |
| | | | | | | MR, | | | | | • | • | • | . , | , | • | • |
| AU | 9882 | • | • | • | | | • | | | AU 19 | 98-8 | 2245 | | 1998 | 0626 | | |
| | | | | | | | | | | EP 19 | | | | | | | |
| | | | | | | | | | | , GR, | | | | | | MC. | PT. |
| | | IE, | • | , | , | , | , | , | | ,, | , | , | , | , | , | , | , |
| дÞ | 2002 | | | Т: | 2 | 2002 | 0312 | | | JP 19 | 99-5 | 0538 | 6 | 1998 | 0626 | | |
| PRIORIT | | | | | _ | | | | | 1997- | | | | | | | |
| LIXIONII | I ALL. | L14. | TIVEO | • • | | | | | - | 1997- | | | | | | | |
| | | | | | | | | | _ | | | | | | _ | | |
| | | | | | | | | | WO | 1998- | GBT8 | 82 | W | 1998 | 1626 | | |

A wound dressing which comprises a carrier layer having a non-adherent to AB cell layer on a wound facing surface thereof is disclosed. The non-adherent layer has bonded thereto a biodegradable cell anchoring layer which anchors mammalian cells. In use, the degradable layer breaks down releasing the cells into the wound site which are discouraged from reattaching to the dressing by the non-adherent layer. Thus, the dressing can switch from a cell binding state to a state in which the binding of cells is discouraged. Systems, methods of treatment and methods of manufg. the dressing are also disclosed. Opsit IV 3000 polyurethane film was exposed to nitrogen plasma and promptly covered with a thin coat of a soln. contg. 20% ethylene glycol diglycidyl ether (I) and 1% CM-cellulose (II). An aq. soln. of 10 mg/mL-heparin was then sprayed on top of I:II acting and the resulting material was dried at 60.degree. for 5 h, then it was sterilized and stored dry. The above film was immersed in fetal calf serum and a suspension of human keratinocytes. Cells adhered to the film within 4-16 h. Following subsequent in vitro culture, the cells detached from the film and were released into the medium.

L16 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS 1998:689255 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 129:281053

Wound dressings containing active substances TITLE: Woessner, Werner; Oswald, Ute; Meister, Frank; INVENTOR(S):

Hueckel, Marion; Mueller, Peter-Juergen; Buehler,

Konrad; Taplick, Thomas

PATENT ASSIGNEE(S): Thueringisches Institut fuer Textil- und

> Kunststoff-Forschung e.V., Germany; Hans Knoell Institut fuer Naturstoff-Forschung e.V.; GWE

Gesellschaft fuer Wissenschaft und Entwicklung m.b.H.;

Gothaplast Verbandpflasterfabrik G.m.b.H.

Ger. Offen., 6 pp. SOURCE:

CODEN: GWXXBX

DOCUMENT TYPE: Patent German LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|------------------|----------|
| | | | | |
| DE 19712699 | A1 | 19981001 | DE 1997-19712699 | 19970326 |
| DE 10712600 | C2 | 20000525 | | |

20000525 DE 19712699 C2 A wound plaster consists of an adhesive-coated backing layer, an overlay AB comprising a dried polysaccharide gel contg. medicinally active substances and excipients, and a removable release liner. The polysaccharide gel is dried by microwave irradn., optionally with the aid of heated gases and/or IR irradn.; this method provides homogeneous drying, without degrdn. of the active agents, to a film which does not have the spongy, mech. weak structure of freeze-dried polysaccharide films. Thus, a mixt. of hyaluronic acid (mol. wt. 1.5 .times. 106) 2, glycerin 2, p-hydroxybenzoic acid 0.06, and distd. water 95.94 parts was continuously applied to the Teflon-coated belt of a film-casting machine and passed through a 6 m-long, 25-kW microwave tunnel at 35 m/h with a countercurrent stream of air at 40-50.degree. to produce a film 240 .mu.m thick. This plasticized hyaluronic acid film was scraped off and layered onto a band of cotton fabric (180 g/m2) at 50.degree.; the fabric band was then placed in the middle of a strip of adhesive-coated backing material and covered with detachable polypropylene film.

=> d ind 2

- L16 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
- ICM A61L015-28 IC
- ICS A61F013-02; A61L015-44; A61F017-00; A61K038-17; C08L005-00
- CC 63-7 (Pharmaceuticals)
- wound adhesive dressing polysaccharide gel; hyaluronate gel drug medical ST dressing
- Medical goods IT
 - (absorbents; wound dressings contg. active substances)
- IT Lipids, biological studies
 - Proteins (specific proteins and subclasses)
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (complexes, with hyaluronic acid; wound dressings contg. active substances)
- IR radiation IT

```
Microwave
        (drying with; wound dressings contg. active substances)
     Polysaccharides, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (gels; wound dressings contg. active substances)
IT
    Gases
        (heated, drying with; wound dressings contg. active substances)
IT
    Absorbents
        (medical; wound dressings contg. active substances)
     Peptide complexes
TΨ
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (with hyaluronic acid; wound dressings contg. active substances)
IT
    Anti-inflammatory drugs
    Antioxidants
    Binders
    Blister
    Cotton fabrics
     Disinfectants
     Dressings (medical)
     Drugs
     Drying
     Emulsifying agents
     Fabrics
    Hydrocolloids
    Hydrogels
    Liposomes (drug delivery systems)
    Permeation enhancers
     Plasticizers
     Preservatives
     Thickening agents
        (wound dressings contg. active substances)
ΙT
    Lymphokines
     Vitamins
    RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (wound dressings contg. active substances)
    Glycosaminoglycans, biological studies
ΙT
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    (wound dressings contg. active substances) 50-81-7, L-Ascorbic acid, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (antioxidant; wound dressings contg. active substances)
     55-56-1D, Chlorhexidine, compds. with glucose
IT
                                                      1837-57-6, Ethacridine
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (disinfectant; wound dressings contg. active substances)
IT
     260-94-6D, Acridine, derivs.
                                     65431-33-6D, Trypaflavine, derivs.
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (dyes; wound dressings contg. active substances)
     56-81-5, 1,2,3-Propanetriol, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (plasticizer; wound dressings contg. active substances)
     110-44-1, Sorbic acid
ΙT
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (preservative; wound dressings contq. active substances)
IT
     99-96-7D, esters
```

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preservatives; wound dressings contg. active substances) ΙT 50-99-7D, D-Glucose, compds. with chlorhexidine 79-83-4, Pantothenic RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (wound dressings contg. active substances) 62-49-7D, Choline, complexes with hyaluronic acid IT 1398-61-4, Chitin 9000-01-5, Gum arabic 9000-07-1, Carrageenan 9000-30-0, Guar gum 9000-65-1, Gum tragacanth 9000-69-5, 1 9004-54-0, Dextran, biological studies 9000-69-5, Pectin 9000-40-2, Locust bean gum 9002-18-0, Agar 9004-32-4 9004-61-9, Hyaluronic acid 9004-61-9D, Hyaluronic acid, derivs. 9004-61-9D, Hyaluronic acid, esters 9005-25-8, Starch, biological 9005-32-7, Alginic acid 9005-49-6, Heparin, biological studies 9007-27-6, Chondroitin 9012-76-4, Chitosan 9050-67-3, Schizophyllan 9057-02-7, Pullulan 9067-32-7, S hyaluronate 11138-66-2, Xanthan gum 39300-88-4, Tara gum 9057-02-7, Pullulan 9067-32-7, Sodium 54724-00-4, Curdlan 69992-87-6, Keratan 71010-52-1, Gellan gum 73613-05-5, Fenugreek gum 75634-40-1, Dermatan 96949-21-2, Rhamsan gum 96949-22-3, Welan gum 111744-92-4, Benzyl hyaluronate 111745-19-8, Ethyl hyaluronate RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (wound dressings contg. active substances)

L16 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1996:725353 HCAPLUS

DOCUMENT NUMBER: 126:51022

TITLE: Gel-forming system for use as wound dressings

INVENTOR(S): Fox, Adrian S.; Allen, Amy E.

PATENT ASSIGNEE(S): Nepera, Inc., USA

SOURCE: U.S., 8 pp.
CODEN: USXXAM

DOCUMENT TYPE: Paten't LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
US 5578661 A 19961126 US 1994-221159 19940331

A gel-forming system comprising an aq. mixt. of a first component of at AB. least one water-sol. polymer in an amt. sufficient to increase the initial viscosity of the mixt. and impart adhesion properties thereto; a second component of an acid-contg. polymer; a third component of an amino-contg. polymer; and water. This system has a pH 5.5-8.5 and the second and third components are each present in sufficient amts. which, in combination, increase the cohesiveness of the mixt. over time, such that the mixt. can be initially combined in a relatively fluid state and subsequently forms a cohesive gel structure. This system is useful as a wound dressing for deep wound cavities because the gel protects the wound and permits healing, does not interfere with new tissue growth or development, is capable of absorbing significant amts. of wound exudate, and has sufficient cohesive strength for subsequent removal from the cavity as an integral plug without interrupting the healing process. For example, a gel-forming compn. contained ethylene-maleic anhydride copolymer 0.5, N,O-carboxymethyl chitosan 2.5, PVP 10, polyethylene oxide 0.5, and NaOH 0.16 %.

=> d hitstr 3

L16 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS
IT 9003-01-4, Polyacrylic acid 9005-49-6, Heparin
, biological studies 25104-18-1, Poly(L-lysine)

25322-68-3, Polyethylene oxide 38000-06-5,

Poly(L-lysine)

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(gel-forming system for use as wound dressings)

RN 9003-01-4 HCAPLUS

CN 2-Propenoic acid, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 79-10-7 CMF C3 H4 O2

о || но-с-сн==сн₂

9005-49-6 HCAPLUS RN

CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

25104-18-1 HCAPLUS RN

L-Lysine, homopolymer (9CI) (CA INDEX NAME) CN

CM

CRN 56-87-1

CMF C6 H14 N2 O2

CDES 5:L

Absolute stereochemistry.

RN

25322-68-3 HCAPLUS Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX CN

$$HO = \begin{bmatrix} CH_2 - CH_2 - O \end{bmatrix}_n$$

38000-06-5 HCAPLUS RN

Poly[imino[(1S)-1-(4-aminobutyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX CN NAME)

=> d ind 3

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L16 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS
     ICM C08L005-00
IC
     ICS C08L039-06; C08L071-02
NCL
     524027000
     63-7 (Pharmaceuticals)
CC
ST
     wound dressing gel polymer mixt
TT
     Dressings (medical)
     Electrolytes
        (gel-forming system for use as wound dressings)
IT
     Glycosaminoglycans, biological studies
     Peptides, biological studies
     Platelet-derived growth factors
     Polysaccharides, biological studies
     Transforming growth factor .beta.1
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (gel-forming system for use as wound dressings)
     526-95-4D, Gluconic acid, derivs.
                                         9000-07-1, Carrageenan
ΙT
                                                                   9002-18-0,
                                         9003-39-8, PVP
     Agar 9003-01-4, Polyacrylic acid
                                                           9004-61-9,
     Hyaluronic acid 9005-32-7, Alginic acid 9005-49-6,
     Heparin, biological studies
                                   9006-26-2, Ethylene-maleic anhydride
                 9011-16-9, Maleic anhydride-methyl vinyl ether copolymer
     copolymer
     9012-76-4, Chitosan 25104-18-1, Poly(L-lysine)
     25322-68-3, Polyethylene oxide
                                       28062-44-4, Acrylic
     acid-vinylpyrrolidone copolymer 38000-06-5, Poly(L-lysine)
     62229-50-9, Epidermal growth factor 83512-85-0, N-Carboxymethylchitosan
     107043-88-9, N,O-Carboxymethylchitosan
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (gel-forming system for use as wound dressings)
     56-81-5, Glycerol, biological studies 96-48-0, .gamma.-Butyryl lactone 97-64-3, Ethyl lactate 123-42-2, Diacetone alcohol 872-50-4,
IT
     N-Methylpyrrolidone, biological studies 2687-91-4, N-Ethylpyrrolidone
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (humectant; gel-forming system for use as wound dressings)
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L16 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1996:369827 HCAPLUS

DOCUMENT NUMBER: 125:35743

TITLE: Modified alginate fibers for wound dressings with

improved absorbancy

INVENTOR(S): Qin, Yimin; Gilding, Keith Dennis PATENT ASSIGNEE(S): Innovative Technologies Limited, UK

SOURCE: PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PA' | PATENT NO. | | | | KIND DATE | | | | APPLICATION NC | | | | | | DATE | | |
|---------|------------|---------|------|-----|-----------|------|------|---------------------------|----------------|------|------|-------|-----|------|----------|-----|-----|
| WO | 9610 | 106 | | A | 1 | 1996 | 0404 | | | | | | | 1995 | 0926 | | |
| | W: | AM, | ΑT, | AU, | BB, | BG, | BR, | BY, | CA, | CH, | CN, | CZ, | DE, | DK, | EE, | ES, | FI, |
| | | GB, | GE, | HU, | IS, | JP, | ΚE, | KG, | KP, | KR, | ΚZ, | LK, | LR, | LT, | LU, | LV, | MD, |
| | | MG, | MK, | MN, | MW, | MX, | NO, | NZ, | PL, | PT, | RO, | RU, | SD, | SE, | SG, | SI, | SK, |
| | | ТJ, | TM | • | | • | - | - | | | • | • | | • | | • | • |
| | RW: | KE, | MW, | SD, | SZ, | UG, | AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | IE, | IT, |
| | | | | | | | | | | | | | | GN, | | | |
| | | SN, | TD, | TG | • | | | | | | | , | · | • | • | · | |
| AU | 9535 | 306 | • | A | 1 | 1996 | 0419 | | А | U 19 | 95-3 | 5306 | | 1995 | 0926 | | |
| GB | 2307 | 687 | | A | 1 | 1997 | 0604 | | G | B 19 | 97-6 | 596 | | 1995 | 0926 | | |
| GB | 2307 | 687 | | B | 2 | 1999 | 0310 | | | | | | | | | | |
| EP | 7836 | 05 | | A | 1 | 1997 | 0716 | | E | P 19 | 95-9 | 3212 | 7 | 1995 | 0926 | | |
| | R: | BE, | DE, | DK, | ES, | FR, | GB, | IT, | LU, | NL, | SE | | | | | | |
| JP | 1050 | 6442 | • | T | 2 | 1998 | 0623 | | Ĵ | P 19 | 95-5 | 11498 | 3 | 1995 | 0926 | | |
| US | 6080 | 420 | | A | | 2000 | 0627 | | U | S 19 | 97-8 | 0968 | 6 | 1997 | 0630 | | |
| PRIORIT | Y APP | LN. | INFO | . : | | | | | GB 1 | 994- | 1957 | 2 | Α | 1994 | 0929 | | |
| | | | | | | | | | GB 1 | 995- | 1514 | | A | 1995 | 0126 | | |
| | | | | | | | | (| GB 1 | 995- | 1693 | 0 | Α | 1995 | 0818 | | |
| | | | | | | | | WO 1995-GB2284 W 19950926 | | | | | | | | | |

AB The title fibers are prepd. by spinning aq. solns. contg. 70-95:5-30 (wt. ratio) mixts. of alginates and water-sol. nonalginate polymers [e.g., polysaccharides, poly(carboxyamino acids), poly(acrylic acid), poly(methacrylic acid) or salts thereof] into a coagulating bath. An aq. dope contg. Na alginate (Protanal LF 10/62) 12, CM-cellulose 1.5, and high-methyloxy pectin 1.5 kg was spun at 12 m/min, taken up at 7.2 m/min, drawn 80.degree., washed, dried, crimped, and cut to give staple fibers suitable for nonwoven wound dressings.

L16 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1995:324872 HCAPLUS

DOCUMENT NUMBER: 122:89477

TITLE: Hydrolytically labile cyanogen halide-crosslinked

polysaccharide microspheres

INVENTOR(S): Smith, Daniel J.; Chakravarthy, Debashish

University of Akron, USA PATENT ASSIGNEE(S): SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2 Patent DOCUMENT TYPE:

English LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

KIND DATE PATENT NO. APPLICATION NO. DATE ______ ---------WO 9427647 A1 19941208 WO 1994-US5702 19940519

W: CA, JP

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LÚ, MC, NL, PT, SE US 5549908 19930520

A 19960827 US 1993-65742 PRIORITY APPLN. INFO.: US 1993-65742 19930520

Water swellable and hydrolytically labile (and therefore potentially biodegradable) non-toxic microspheres or beads comprise a polysaccharide (e.g. dextran) crosslinked with a cyanogen halide (e.g. cyanogen bromide) in an aq. alk. medium which is a disperse phase of a water-in-oil dispersion. The microspheres are useful in the treatment of wounds, in particular as an absorptive agent for wound exudates. The microspheres may be formed into a wound dressing which includes a blend of the microspheres and a hydrophobic adhesive matrix material on a waterproof backing sheet.

=> d hitstr ind 5

L16 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS

9042-14-2P, Dextran sulfate IT

> RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (crosslinked; swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

9042-14-2 HCAPLUS RN

CN Dextran, hydrogen sulfate (9CI) (CA INDEX NAME)

CM

CRN 9004-54-0 CMF Unspecified CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 7664-93-9 CMF H2 O4 S

IC ICM A61L015-00

CC 63-6 (Pharmaceuticals)

ST cyanogen halide crosslinking polysaccharide microsphere bead; wound dressing crosslinking polysaccharide microsphere bead

IT Polysaccharides, biological studies

RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(crosslinked; swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

IT Crosslinking agents

(cyanogen halides; swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

IT Pharmaceutical dosage forms

(beads, swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

IT Medical goods

(dressings, swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

IT Pharmaceutical dosage forms

(microspheres, swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

IT 74-79-3DP, Arginine, grafts with dextran 9004-54-0P, Dextran, biological studies 9042-14-2P, Dextran sulfate

RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(crosslinked; swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

IT 506-68-3, Cyanogen bromide

RL: RCT (Reactant)

(crosslinking agent; swellable and hydrolytically labile crosslinked polysaccharide microspheres for wound dressings)

=> d ibib abs 6

L16 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1994:563976 HCAPLUS

DOCUMENT NUMBER: 121:163976

TITLE: Heparin-fibroblast growth factor-fibrin

complex: in vitro and in vivo applications to

collagen-based materials

AUTHOR(S): DeBlois, Chantal; Cote, Marie-France; Doillon, J.

CORPORATE SOURCE: Laval University, Quebec, PQ, G1L 3L5, Can.

Biomaterials (1994), 15(9), 665-72 CODEN: BIMADU; ISSN: 0142-9612 SOURCE:

DOCUMENT TYPE: Journal LANGUAGE: English

Biol. mols. such as fibrin and growth factors could have interesting AB features to design bioactive biomaterials and particularly collagen-based materials used as connective tissue replacement. Different combinations of fibroblast growth factor (FGF) and heparin complexes to fibrin were analyzed. In vitro, FGF bound to matrix was rapidly, but partially released, specifically with heparin. Heparin concns. were progressively equilibrated between matrix and medium. DNA replication of fibroblasts grown either on or within fibrin matrixes was increased in the presence of both FGF and high doses of heparin incorporated in fibrin. S.c. implantations of collagen sponges impregnated with composite fibrin matrixes showed qual. and quant. tissue ingrowth within the sponges. The noncrosslinked collagen of fibrin-impregnated sponges swelled after implantation. The resulting fibroblast-infiltrated tissue resembled a normal dense connective tissue that was obsd. particularly in the presence of high doses of heparin and FGF incorporated in fibrin.

=> d ibib abs 2

L18 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1997:803512 HCAPLUS

DOCUMENT NUMBER: 128:66528

TITLE: Absorptive wound dressing for wound healing promotion

INVENTOR(S): Donovan, Maura G.; Keogh, James R.; Holmblad, Carolann

Μ.

PATENT ASSIGNEE(S): Medtronic, Inc., USA

SOURCE: U.S., 7 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

KIND DATE PATENT NO. APPLICATION NO. DATE ----------19971209 US 1994-241120 19940510 US 5695777 A A wound dressing for use with exuding wounds includes (a) an outer AB vapor-permeable layer permitting transpiration of fluid from the dressing; (b) an intermediate layer of hydrogel adapted for absorbing wound exudate; (c) a wound-contacting layer for sepg. the intermediate hydrogel layer from the wound; (d) wicking means assocd. with the wound-contacting layer for conducting exudate from the wound to the hydrogel; and (e) a therapeutic agent retained in the dressing by the wound-contacting layer. An advantage of the invention lies in the use of an absorptive hydrogel which does not directly contact the wound and the hydrogel may be tailored to the needs of specific wounds through the inclusion of therapeutic agents such as antimicrobials which remain largely undelivered to the wound site and yet provide an environment which inhibits microbial growth.

=> d ibib abs 3

L18 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1994:563976 HCAPLUS

DOCUMENT NUMBER: 121:163976

TITLE: Heparin-fibroblast growth

factor-fibrin complex: in vitro and in vivo applications to collagen-based materials

AUTHOR(S): DeBlois, Chantal; Cote, Marie-France; Doillon, J.

CORPORATE SOURCE: Laval University, Quebec, PQ, G1L 3L5, Can.

SOURCE: Biomaterials (1994), 15(9), 665-72

CODEN: BIMADU; ISSN: 0142-9612

DOCUMENT TYPE: Journal LANGUAGE: English

Biol. mols. such as fibrin and growth factors could have interesting features to design bioactive biomaterials and particularly collagen-based materials used as connective tissue replacement. Different combinations of fibroblast growth factor (FGF) and heparin complexes to fibrin were analyzed. In vitro, FGF bound to matrix was rapidly, but partially released, specifically with heparin. Heparin concns. were progressively equilibrated between matrix and medium. DNA replication of fibroblasts grown either on or within fibrin matrixes was increased in the presence of both FGF and high doses of heparin incorporated in fibrin. S.c. implantations of collagen sponges impregnated with composite fibrin matrixes showed qual. and quant. tissue ingrowth within the sponges. The noncrosslinked collagen of fibrin-impregnated sponges swelled after implantation. The resulting fibroblast-infiltrated tissue resembled a normal dense connective tissue that was obsd. particularly in the presence of high doses of heparin and FGF incorporated in fibrin.

=> d ibib abs 4

L18 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1990:597915 HCAPLUS

DOCUMENT NUMBER: 113:197915

TITLE: In vitro properties of crosslinked, reconstituted

collagen sheets

AUTHOR(S): Morykwas, Michael J.

CORPORATE SOURCE: Bowman Gray Sch. Med., Wake Forest Univ.,

Winston-Salem, NC, 27103, USA

SOURCE: J. Biomed. Mater. Res. (1990), 24(8), 1105-10

CODEN: JBMRBG; ISSN: 0021-9304

DOCUMENT TYPE: Journal LANGUAGE: English

Reconstituted, 100-.mu.m-thick collagen sheets were crosslinked with either UV light, Cr, or cysteine for use as a burn covering. The sheets were also exposed to a "surface agent" (hydroxyproline, fibronectin, or sol. basement membrane matrix contg. Type IV collagen) as a preliminary step in planned adherence studies. Since some chems. render the collagen toxic, the modified sheets were tested for cytotoxicity using human keratinocytes and fibroblasts. Autoradiog. and 3H-thymidine incorporation were used to quantitate the proliferative rate of these cells in vitro. There was a universal depression of keratinocyte incorporation of 3H-thymidine following a 1-day exposure to any collagen sheet when compared to cells not exposed to any collagen. This effect had lessened by 5 days' exposure to the collagen. Conversely, the fibroblasts showed an enhancement in rate of incorporation after 1-day exposure, esp. for cells exposed to collagen sheets crosslinked by UV light. This effect had also lessened by 5 days' exposure. Autoradiog. showed few variations for any of the cells exposed for either time period. Cr leaching was detd., with no values >30% of the allowable max. set by both the British and American Pharmacopeia.

=> d bib abs 1

- L15 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
- AN 1997:172380 HCAPLUS
- DN 126:176939
- TI Moisture-holding films or sheets for manufacturing wound dressings and other products
- IN Inaba, Yukitake; Usami, Takeshi; Yokomori, Yorozu
- PA Kyowa Hakko Kogyo Kk, Japan
- SO Jpn. Kokai Tokkyo Koho, 5 pp. CODEN: JKXXAF
- DT Patent
- LA Japanese
- FAN.CNT 1

ΡI

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| | | | | |
| JP 09010294 | A2 | 19970114 | JP 1995-165846 | 19950630 |

AB Films or sheets showing high vapor permeability, water absorbability and moisture-holding activity are prepd. from synthetic **polypeptides** such as poly-.gamma.-methyl-L-glutamate and polysaccharides (mucopolysaccharides) such hyaluronic acid. The films or sheets are useful for manufg. e.g. wound dressings and diapers.

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L15
     ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ΑN
     1993:525199 HCAPLUS
DN
     119:125199
ΤI
     Crosslinkable polysaccharides, polycations and lipids useful for
     encapsulation of drugs and cells and manufacture of wound dressings
     Soon-Shiong, Patrick; Desai, Neil P.; Sandford, Paul A.; Heintz, Roswitha
ΙN
     A.; Sojomihardjo, Soebianto
PA
     Clover Consolidated, Ltd., Switz.
SO
     PCT Int. Appl., 53 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 2
     PATENT NO.
                      KIND
                            DATE
                                            APPLICATION NO.
                                                             DATE
ΡI
     WO 9309176
                       Α2
                             19930513
                                            WO 1992-US9364
                                                             19921029
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WO 9309176 ΑЗ 19930722 AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG AU 9331247 Α1 19930607 AU 1993-31247 19921029 EP 610441 Α1 19940817 EP 1992-925046 19921029 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE US 5837747 A 19981117 US 1994-232054 19940428 PRAI US 1991-784267 19911029 WO 1992-US9364 19921029

AB Crosslinkable polysaccharides, polycations and lipids which are capable of undergoing free radical polymn. are used for encapsulation of drugs, biol. materials and cells, as well as manuf. of bioadhesives and wound dressing. Alginic acid was reacted with acryloyl chloride in presence of Et3NH2 under N for 24h to obtain alginate acrylate (I). A polymd. crosslinked gel was prepd. contg. I 0.1, acrylamide 0.1, water 3.75, glycerol 1.25, methylene bisacrylamide 0.01g. The gels can be prepd. as flat sheets that can be applied to wounds.

L52 ANSWER 1 OF 14 USPATFULL

ACCESSION NUMBER:

2002:22131 USPATFULL

TITLE:

18 Human secreted proteins

INVENTOR(S):

Shi, Yanggu, Gaithersburg, MD, UNITED STATES Young, Paul E., Gaithersburg, MD, UNITED STATES Ebner, Reinhard, Gaithersburg, MD, UNITED STATES Soppet, Daniel R., Centreville, VA, UNITED STATES

Ruben, Steven M., Olney, MD, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: APPLICATION INFO.:

US 2002012966 A1 20020131 US 2001-768826 A1 20010125

RELATED APPLN. INFO.:

20010125 (9)

Continuation-in-part of Ser. No. WO 2000-US22350, filed

on 15 Aug 2000, UNKNOWN

NUMBER DATE ______

PRIORITY INFORMATION:

US 1999-148759P 19990816 (60)

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE,

ROCKVILLE, MD, 20850

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

23

LINE COUNT:

18157

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic

L52 ANSWER 1 OF 14 USPATFULL

SUMM

. . of cancer, as well as, developmental and immune disorders. For example, the proteins can be administered therapeutically to inhibit or reverse the development of tumors. Antibodies to the proteins can be used in diagnostic tests for conditions associated with protein expression. .

SUMM

. . . treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus this protein may modulate apoptosis or tissue differentiation and would be useful in the detection, treatment, and/or prevention of degenerative or proliferative conditions and diseases. The protein is useful in modulating the immune response to aberrant polypeptides, as may exist in proliferating and cancerous cells and tissues. The protein can also.

SUMM

. . . to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies

directed against the protein. .

SUMM . . . used to determine biological activity, raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. . .

SUMM . . . used to determine biological activity, raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. . .

SUMM . . . (1998)); all information available through these references are hereby incorporated by reference herein.). Leptin plays a pivotal role in the **modulation** of neuronal and hormonal systems involved in the regulation of body weight and reproductive functions. Additionally, the translation product of. . .

SUMM . . . to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. . .

SUMM . . . is thought to be important in cell signaling. The Toll-related proteins can be used to alter phosphate metabolism and in modulation of inflammatory function and innate immune responses. The Toll-related proteins can also be used in the treatment of conditions exhibiting. . .

SUMM . . . to Toll proteins indicates that polynucleotides and polypeptides corresponding to this gene are useful for altering phosphate metabolism and in **modulation** of inflammatory function and innate immune responses.

SUMM . . . treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus this protein may modulate apoptosis or tissue differentiation and would be useful in the detection, treatment, and/or prevention of degenerative or proliferative conditions and diseases. The protein is useful in modulating the immune response to aberrant polypeptides, as may exist in proliferating and cancerous cells and tissues. The protein can also. . .

SUMM . . . to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. . .

SUMM . . . to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. . .

SUMM . . . treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus this protein may modulate apoptosis or tissue differentiation and would be useful in the detection, treatment, and/or prevention of degenerative or proliferative conditions and diseases. The protein is useful in modulating the immune response to aberrant polypeptides, as may exist in proliferating and cancerous cells and tissues. The protein can also. . . to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. . .

. . all references available through this accession are hereby SUMM incorporated by reference herein.) which is functionally associated with the IL-4 receptor, modulates B cell phenotype and is a novel member of the human macrophage mannose receptor family. The tissue distribution and homology to GP200-MR6 protein SUMM indicates that polynucleotides and polypeptides corresponding to this gene are useful for modulating B cell phenotype. The tissue distribution in dendritic cells indicates that the polynucleotides and polypeptides corresponding to this gene would. SUMM . . to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. . . . used to determine biological activity, raise antibodies, as SUMM tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. . . . treating, detecting, and/or preventing said disorders and SUMM conditions, in addition to other types of degenerative conditions. Thus this protein may modulate apoptosis or tissue differentiation and would be useful in the detection, treatment, and/or prevention of degenerative or proliferative conditions and diseases. The protein is useful in modulating the immune response to aberrant polypeptides, as may exist in proliferating and cancerous cells and tissues. The protein can also. . . to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. SUMM . . to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. gene are useful for diagnosis and/or treatment of cancer. For example, the proteins can be administered therapeutically to inhibit or SUMM reverse the development of tumors. The tissue distribution in brain also indicates that the polynucleotides and polypeptides corresponding to this gene. . . treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus this protein may modulate apoptosis or tissue differentiation and would be useful in the detection, treatment, and/or prevention of degenerative or proliferative conditions and diseases. The protein is useful in modulating the immune response to aberrant polypeptides, as may exist in proliferating and cancerous cells and tissues. The protein can also. . to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. SUMM . . . tumorogenesis. Hepatoma-derived growth factor(HDGF), has been recently cloned (Nakamura, H. et al., J. Biol. Chem., 269(40):25143-25149 (1994)). HDGF is a heparin-binding protein which is mitogenic for fibroblasts. HDGF was purified from the conditioned medium of a human hepatoma-derived cell line, HuH-7 by tritiated thymidine incorporation into Swiss.

. . . gene are useful for diagnosis and/or treatment of cancer. For

SUMM

example, the proteins can be administered therapeutically to inhibit or reverse the development of tumors. The expression within fetal tissue and other cellular sources marked by proliferating cells indicates this protein. . . treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus this protein may modulate apoptosis or tissue differentiation and would be useful in the detection, treatment, and/or prevention of degenerative or proliferative conditions and diseases. The protein is useful in modulating the immune response to aberrant polypeptides, as may exist in proliferating and cancerous cells and tissues. The protein can also. .

SUMM

. . . used to determine biological activity, raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that **modulate** their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. . .

SUMM

. . . Hepatoma-derived growth factor (HDGF), has been recently cloned (Nakamura, H. et al., J. Biol. Chem., 269(40):25143-25149 (1994)). HDGF is a heparin-binding protein which is mitogenic for fibroblasts. HDGF was purified from the conditioned medium of a human hepatoma-derived cell line, HuH-7 by tritiated thymidine incorporation into Swiss. . .

SUMM

For example, the proteins can be administered therapeutically to inhibit or reverse the development of tumors. The expression within fetal tissue and other cellular sources marked by proliferating cells indicates this protein. . . treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus this protein may modulate apoptosis or tissue differentiation and would be useful in the detection, treatment, and/or prevention of degenerative or proliferative conditions and diseases. The protein is useful in modulating the immune response to aberrant polypeptides, as may exist in proliferating and cancerous cells and tissues. The protein can also. .

SUMM

. . . to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that **modulate** their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. . .

SUMM

. . . tetramers. IL-16 requires the expression of CD4 for its functions, which include induction of chemotaxis, interleukin-2 receptor and HLA-DR expression, **reversible** inhibition of TcR/CD3-dependent activation and induction of a repressor of HIV-1 transcription. It represents a major source of the lymphocyte. . .

SUMM

. . . used to determine biological activity, raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein. . .

SUMM

conditions, in addition to other types of degenerative conditions. Thus this protein may modulate apoptosis or tissue differentiation and would be useful in the detection, treatment, and/or prevention of degenerative or proliferative conditions and diseases. The protein is useful in modulating the immune response to aberrant polypeptides, as may exist in proliferating and cancerous cells and tissues. The protein can also. . . to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or

receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein.

SUMM . . . treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus this protein may modulate apoptosis or tissue differentiation and would be useful in the detection, treatment, and/or prevention of degenerative or proliferative conditions and diseases. The protein is <-----User Break----->
u =>

L52 ANSWER 2 OF 14 USPATFULL

ACCESSION NUMBER: 2001:212417 USPATFULL

TITLE: In situ bioreactors and methods of use thereof
INVENTOR(S): Pierce, Glenn, Rancho Santa Fe, CA, United States

Chandler, Lois Ann, Encinitas, CA, United States

NUMBER DATE

PRIORITY INFORMATION: US 1999-168470P 19991201 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH

AVE, SUITE 6300, SEATTLE, WA, 98104-7092

NUMBER OF CLAIMS: 104 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 3 Drawing Page(s)

LINE COUNT: 2302

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides in situ bioreactors comprising a biocompatible substance comprising nucleic acid molecules and capable of cellular ingrowth and systemic delivery of a bioactive agent. Also provided are compositions, devices, and kits comprising the same. In various embodiments the biocompatible substance comprises a matrix and at least one nucleic acid molecule encoding a bioactive agent. In other embodiments bioreactors are provided wherein a first gene that encodes a growth factor is present and a second gene encoding a bioactive agent is present during manufacture or provided to the bioreactor following manufacture or implantation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 2

L52 ANSWER 2 OF 14 USPATFULL

DETD . . . only for a short duration of time. The matrices may take the form of sponges, implants, tubes, telfa pads, band-aids, bandages, fibers, hollow fibers, sutures, pads, lyophilized components, gels, patches, powders, porous compositions, or nanoparticles. In addition, matrices can be designed. . .

DETD . . . been widely used in medical applications are poly(paradioxanone) (PDS), poly(lactic acid) (PLA), poly(glycolic acid) (PGA), and PLGA copolymers. Copolymerization enables modulation of the degradation time of the material. By changing the ratios of crystalline to amorphous polymers during polymerization, properties of.

DETD . . . sutures. In certain embodiments of the invention, such medical devices and other matrices may be coated with nucleic acids and/or polypeptides using conventional coating techniques as are well known in the art. Such methods include, by way of example and not limitation, dipping the. . .

DETD . . . adenosine deaminase, factor XIII, Protein C, Protein S, an

interleukin, an interferon, insulin, tissue plasminogen activator, plasminogen, plasmin, urokinase, streptokinase, heparin, thrombomodulin, and Protein C activating agents. An exemplary, and in no way wholly inclusive, listing is provided in Table I. . . Lawn, PNAS 78:5435, 1981

h-gDNA Todokoro, EMBO J. 3:1809, 1984 h-gDNA Torczynski, PNAS 81:6451, 1984 Taniguchi, Gene 10:11, 1980 Lawn, Nuc. Acid Res. interferon, beta h-cDNA h-gDNA (fibroblast) 9:1045, 1981

Sehgal, PNAS 80:3632, 1983 Sagar, Sci. 223:1312, 1984 h-gDNA (related) h-gDNA (related)

V00546,. . .

L52 ANSWER 3 OF 14 USPATFULL

ACCESSION NUMBER: 2001:75536 USPATFULL

TITLE:

Heparin binding mitogen with homology to epidermal

growth factor (EGF)

INVENTOR(S):

Klagsbrun, Michael, Newton, MA, United States Abraham, Judith A., San Jose, CA, United States

Higashiyama, Shigeki, Osaka, Japan

Besner, Gail E., Buffalo, NY, United States

PATENT ASSIGNEE(S):

Scios Nova, Inc., Mountain View, CA, United States

(U.S. corporation)

The Children's Medical Center Corporation, Boston, MA,

United States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION:

US 6235884 B1 20010522 US 1998-158710 19980922 (9)

APPLICATION INFO.: RELATED APPLN. INFO.:

Division of Ser. No. US 1993-39364, filed on 15 Jun

1993, now patented, Pat. No. US 5811393

Continuation-in-part of Ser. No. US 598082, now

abandoned

DOCUMENT TYPE:

Utility Granted

FILE SEGMENT: PRIMARY EXAMINER:

Allen, Marianne P.

LEGAL REPRESENTATIVE:

Fish & Richardson P.C.

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

1

NUMBER OF DRAWINGS:

5 Drawing Figure(s); 5 Drawing Page(s)

LINE COUNT:

1411

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are heparin binding mitogens which include an epidermal growth factor-homologous segment (HB-EHM). These factors stimulate proliferation of fibroblast cells, epithelial cells, and smooth muscle cells, but not endothelial cells. Also disclosed are isolated antibodies that recognize, and purified nucleic acids that encode, the above growth factors as well as isolated polypeptides, vectors containing such nucleic acids, and cells harboring such vectors. Growth factors of this invention may be used for accelerating the rate of wound healing, for the in vitro culture of HB-EHM-responsive cells, and for the identification of antagonists to HB-EHM.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 3

L52 ANSWER 3 OF 14 USPATFULL

Disclosed are heparin binding mitogens which include an epidermal growth factor-homologous segment (HB-EHM). These factors stimulate proliferation of fibroblast cells, epithelial cells, and smooth muscle cells, but not endothelial cells. Also disclosed are isolated antibodies that recognize, and purified. . .

SUMM Heparin affinity chromatography has been used extensively for purifying and characterizing a variety of these growth factors. Acidic FGF (aFGF) and basic FGF (bFGF) bind to immobilized heparin columns and are eluted with 1.0M to 1.2M NaCl and 1.5M to 1.8M NaCl, respectively (Folkman and Klagsbrun, 235 Science. . . Biol. Chem.

1924, 1986). Several growth factors which are structurally homologous to aFGF and bFGF also have an affinity for heparin (see, for example, Rubin et al., 86 Proc. Natl. Acad. Sci. USA 802, 1989). PDGF binds to immobilized heparin, but with relatively low affinity, being eluted with only 0.5M NaCl. Epidermal growth factor (EGF) does not bind heparin to any substantial extent under the conditions described in the cited references on heparin binding growth factors. Lobb et al. (261 J. Biol. Chem. 1924, 1986) report the partial purification by heparin affinity of two classes of growth factors mitogenic for endothelial cells. Gospodarowicz et al. (81 Proc. Natl. Acad. Sci. USA 6963, 1984) report the use of heparin affinity in the purification of bovine brain and pituitary fibroblast growth factors. Shing et al. (29 J. Cell Biochem. 275, 1985) report a chondrosarcoma-derived growth factor purified by heparin-Sepharose affinity chromatography and Bio Rex 70 cation exchange chromatography. Bohlen et al. (185 FEBS Lett. 177, 1985) report a ${f fibroblast}$ growth factor, derived from human brain, which is purified by cation-exchange chromatography, heparin-Sepharose affinity, and reverse-phase HPLC. Shing et al. (223 Science 1296, 1984) report a heparin-binding tumor cell-derived capillary endothelial cell factor. Besner et al. (107 J. Cell Biol. 481a, 1988) report the detection of a heparin -binding, mononuclear cell-derived growth factor(s) which is cationic, is of 6000-14,000 MW, is inactivated by heat (100.degree. C., 10 min),

SUMM In a second aspect, the invention features polypeptides which bind heparin, which include an EGF-homologous segment, and which stimulate growth of fibroblast cells, epithelial cells, and smooth muscle cells, but not endothelial cells.

- DETD Conditioned medium was assayed for growth factor activity directly, as described below, using either fibroblasts (i.e., BALB/c mouse 3T3 cells), epithelial cells (i.e., human keratinocytes), or smooth muscle cells (i.e., bovine aortic smooth muscle cells, BASMC). Alternatively, CM was first fractionated by fast protein liquid chromatography (FPLC, Pharmacia, Piscataway, N.J.) by applying 500 ml of the CM to a TSK-heparin 5PW column (8.times.75 mm, TOSOHAAS, Philadelphia, Pa.). The column was washed with 10 column volumes of equilibration buffer (0.2M NaCl,. . .
- DETD . . . the three step purification outlined above (and eluting from the TSK-heparin column at 1-1.2M NaCl) was applied to a C.sub.4 reversed phase high performance liquid chromatography column (RP-HPLC). A Beckman model 334 HPLC system was used (Beckman Instruments, Inc., Somerset, N.J.). The sample was loaded onto the C.sub.4 -reversed phase HPLC column (4.6.times.250 mm, Vydac) after equilibration of the column with 5% acetonitrile, 0.1% trifluoroacetic acid. The column was. . .
- DETD . . . the protein, approximately 1.7 ug of protein obtained after cation exchange, copper-affinity, and heparin-affinity chromatography and two cycles of C.sub.4 -reversed phase HPLC of 20 L of conditioned medium were loaded onto an Applied Biosystems gas-phase protein sequencer. Twenty rounds of . . .
- DETD . . . a five minute incubation at room temperature between each addition. The protein mixture was desalted by passage through a C.sub.4 -reversed phase HPLC column, dried, resuspended in 200 .mu.l of 100 mM ammonium bicarbonate, and digested with 0.5 .mu.g of trypsin. . . added, and the reaction was incubated for two additional hours at 27.degree. C. Digestion products were separated on a C.sub.18 -reversed phase HPLC (RP-HPLC) column and subjected to amino terminal sequencing.
- DETD . . . 25 mM followed by incubation of the reaction mixture for 30

minutes at room temperature. After desalting on a C.sub.18 **reversed** phase HPLC column (4.6.times.150 mm, Vydac; gradient of 10% to 40% acetonitrile in 0.1% trifluoroacetic acid), the protein was dried. . .

- DETD . . . with O-glycanase lowered the apparent molecular weight of HB-EHM from 18-20 kDa to about 14-16 kDa (as judged by polyacrylamide gel electrophoreses) suggesting that this polypeptide was modified extensively by O-linked glycosylation.
- DETD . . . purification of the recombinant HB-EHM was accomplished by loading the 2M elute from the heparin-Sepharose column onto a Vydac C.sub.4 reversed-phase column (1 cm.times.25 cm) equilibrated with 15% acetonitrile in 0.1% trifluoroacetic acid, and then eluting the bound protein with a. . .
- DETD . . . growth factors to the injured site will also be used as will the combination of such growth factors with topical bandages, or dressings, or sutures/staples, and with topical creams and ointments, such as the antibacterial Silvadene (Marion Labs, Kansas City, Mo.), commonly used. . .

L52 ANSWER 4 OF 14 USPATFULL

2000:137849 USPATFULL ACCESSION NUMBER:

TITLE: Medicaments containing gelatin cross-linked with

oxidized polysaccharides

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Innogenetics N.V., Belgium (non-U.S. corporation) PATENT ASSIGNEE(S):

NUMBER KIND DATE US 6132759 20001017 WO 9741899 19971113 PATENT INFORMATION: US 1998-180057 APPLICATION INFO.: 19981027 (9) WO 1997-EP2279 19970505 19981027 PCT 371 date 19981027 PCT 102(e) date

NUMBER DATE

PRIORITY INFORMATION: EP 1996-870059 19960503

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Kulkosky, Peter F.

LEGAL REPRESENTATIVE: Bierman, Muserlian and Lucas

NUMBER OF CLAIMS: 17

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 26 Drawing Figure(s); 15 Drawing Page(s)

LINE COUNT: 1841

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a wound dressing comprising a biopolymer matrix comprising gelatin cross-linked with an oxidized polysaccharide. Preferably said oxidized polysaccharide comprises an oxidized dextran or an oxidized xanthan. Preferably said matrix is in the form of a hydrated film, a hydrated or dry foam, dry fibers which may be fabricated into a woven or non-woven tissue, hydrated or dry microbeads, dry powder; or said matrix is covered with a semipermeable film, so as to control the humidity of the wound covered with the dressing, with the permeability chosen so as to maintain this humidity within a therapeutically optimal window. A polysulfated polysaccharide with a M.W. greater than 30,000 kDa is mechanically entrapped during the formation of said matrix.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 4

L52 ANSWER 4 OF 14 USPATFULL

AB The present invention relates to a wound dressing comprising a biopolymer matrix comprising gelatin cross-linked with an oxidized polysaccharide. Preferably said oxidized polysaccharide comprises an oxidized dextran or. . . said matrix is covered with a semipermeable film, so as to control the humidity of the wound covered with the dressing, with the permeability chosen so as to maintain this humidity within a therapeutically optimal window. A polysulfated polysaccharide with a. .

SUMM . . . When loaded with suitable growth factors or wound repair promoting substances, the matrix is useful for the fabrication of wound dressings for the treatment of a variety of wound types, particularly chronic wounds and burns.

. optimal healing. The beneficial effect of covering wounds is SUMM situated at different levels and is dependent on the type of dressing material used. First, especially with acute wounds, suitable dressings may help to achieve haemostasis and thus control blood loss. Secondly, covering effectively shields the wound from the environment, thus protecting it from microbial contamination. Furthermore, some so-called occlusive or semi-occlusive wound dressings have the capability of maintaining the wound moist, which is beneficial for healing. Finally, some wound dressings may themselves directly promote the healing process, for instance because they contain components which directly promote cell growth or migration or which attract or activate cells from the immune system which on their turn secrete growth-promoting substances. Other dressings may contain antimicrobial substances, which are helpful to control infection of the wound.

SUMM Over time, a surprisingly wide variety of **dressing** materials have been used for wound covering, many of which are currently commercially available. Each of them has its own. . .

SUMM Cotton gauze, for instance, is widely used as wound dressing. It has the advantage of being cheap, but the disadvantage of being not occlusive and sometimes becoming encrusted into the wound. To prevent this, these dressings are sometimes impregnated with a greasy substance, such as paraffin. A commercially available example of such a dressing is Jelonet.TM. (Smith and Nephew, UK).

Another class of wound **dressings** are the absorptive hydrogel **dressings**. These have no occlusive properties, but have a high capacity for the absorption of exudate and slough. They consist of. . . which swell upon contact with wound fluid and can absorb several times their own weight of exudate. Commercially available hydrogel **dressings** include Intrasite gel (Smith and Nephew, UK) and Vigilon (CR Bard, USA). A special type of hydrogels are the alginates,.

Another type of dressings are the occlusive or semi-occlusive dressings. In their simplest form, they usually exist of a thin, flexible plastic membrane, e.g. from polyurethane. To facilitate application, these dressings are usually fabricated with a self-adhesive coating. These dressings are called occlusive because they limit water evaporation from the wound surface, thus keeping it moist. Examples of such dressings are Opsite (Smith and Nephew, UK) and Tegaderm (3M, USA). Examples of semi-occlusive dressings are Omiderm (latro Medical Systems, UK) and Exkin (Koninklijke Utermohlen, The Netherlands). The latter dressings allow a slightly higher evaporation rate, resulting in a semi-dry wound surface.

A more complex type of occlusive dressings are the hydrocolloid (HCD) dressings. These are made up of hydrocolioid particles (e.g. consisting of gelatin, pectin, etc.) embedded in a hydrophobic matrix (e.g. a polyisobutylene). These dressings may be backed with an occlusive membrane and/or a foam plastic layer. In addition to being occlusive, HCD dressings have a high absorptive capacity, making them very suitable for the treatment of wounds producing high amounts of exudate. These beneficial properties have made HCD dressings among the most successfully used dressings for the treatment of chronic ulcerations of the skin. Commercially available examples of these dressings include Duoderm.degree. (Convatec, UK) and Tegasorb.TM. (3M, USA).

Although highly successful, recent reports suggest that HCD SUMM dressings may nevertheless induce undesirable side reactions in the treated tissues. For example, Van Luyn reports that Duoderm E (Convatec, UK), Biofilm (Biotrol SPA, France), Comfeel (Coloplast, Denmark) and Ulcer dressing (Johnson and Johnson, USA), all of which are HCD dressings, fall within the high toxicity class when tested in a methylcellulose assays using human skin fibroblasts as target cells (Van. . . University Groningen, The Netherlands; Van Luyn, M., Abstract Book of the joint WHS/ETRS meeting, Amsterdam, 1993 p114). All the HCD dressings tested by this author highly inhibited cell growth (>70%) and induced strongly deviant morphologies in the surviving cells. Leek et al. (Abstract Book of the Second Annual WHS Meeting, Richmond, Va., USA, p75, 1992) have tested four HCD dressings in full-thickness excisional wounds in pigs. All dressings induced development of granulomatous lesions between 4 and 10 days post wounding and exhibiting little evidence of resolution obtained with Duoderm and Intrasite HCD. Rosdy and Clauss (J. Biomedical Mat. Res. 24, 363-3777, 1990) found that the HCD dressing Granuflex.TM. (Bristol-Myers Squibb, USA) induced cytopathic effects on MRC5 fibroblasts and epidermal cells upon direct contact. Young et al. (J.. . model system the development of deep-seated foreign body type reactions and granulomata in healed wounds which were treated with HCD dressings. Our own experiments with the HCD dressing Duoderm.TM. show that this dressing results in a marked and chronic inflammatory response when placed in full thickness wounds in pigs. SUMM The above mentioned data suggest that, while HCD dressings may promote wound healing in the short term, their use is often associated with undesirable inflammatory effects. Therefore, it is clear that there is a need for a wound dressing displaying the beneficial properties of HCD dressings, yet resulting in substantially less chronic inflammation or foreign body response. Such a wound dressing would stimulate granulation tissue formation, be absorptive and preferably be biodegradable within a limited time frame. SUMM Gelatin, which is a denatured form of the protein collagen, has been used in a variety of wound dressings. Since gelatin gels have a relatively low melting point, they are not very stable at body temperature. Therefore, it is. . . the non cross-linked variety was not. Therefore, despite their beneficial haemostatic properties, these products are not very optimal as wound dressings for the treatment of problematic wounds such as chronic ulcers or burns. Consequently, a gelatin-based wound dressing which uses a different, less toxic, cross-linking technology would be very desirable. Dextran is a polysaccharides which is also widely used for medical purposes, and which may also be used in a wound dressing. For example, PCT publication number WO 94/27647 (Smith and Chakravarty) teaches the fabrication of a polymer composition comprised of cross-linked. . . where the cross-linking groups consist of linear imido carbonate or carbonate groups. This polymer can be incorporated in a wound dressing. An important feature of this polymer composition is that it is hydrolytically labile. This means that hydrated forms of the. Apart from the development of improved dressings, increasing SUMM attention has been given over the last years to the possible use of growth factors to promote the healing. . . . the production of physical PLG/peptide mixtures (e.g. by SUMM

. . uses a different, less toxic, cross-linking technology would be

compression moulding of powder mixes), these may be less suitable as

wound dressings because of their rigidity and brittleness.

very desirable for the fabrication of, for instance, growth

SUMM

factor-medicated wound dressings.

- SUMM The present invention thus aims at providing a suitable wound dressing.
- SUMM The present invention further aims at methods for producing and using said wound **dressings** or said controlled or slow release devices.
- SUMM . . . present invention relates to the unexpected finding that polymers comprising gelatin cross-linked with oxidized polysaccharides constitute excellent medicament such as **dressings** for the treatment of wounds. The cross links are formed by Schiff base formation between free amino groups of the. . .
- SUMM . . . on the wound site in an intact form for a sufficiently long time. Another advantage is that the disclosed wound **dressing** has substantially reduced cytotoxical and inflammatory properties as compared with existing gelatin-based materials. This is exemplified in examples 3-5. Yet. . . highly desirable for the treatment of chronic wounds. A further advantage is that one of the embodiments of the disclosed **dressing** offers the possibility to immobilize sulfated dextrans or similar poly-anionic molecules into the **dressing**, a modification which enhances the binding of incorporated or local heparin binding wound repair **modulating** factors.
- SUMM . . . peptide). Such medicated GDP matrices may be used for several therapeutical applications, in particular for the fabrication of medicated wound **dressings**, e.g. by loading them with growth factors or other wound repair-enhancing substances.
- SUMM . . . prepared in this way are useful for a variety of therapeutical applications, in particular for the fabrication of medicated wound dressings.
- SUMM In a preferred embodiment, the proposed wound **dressing** consists of a hydrated sheet or film of matrix as defined above, backed with an occlusive or semi-occlusive film. Occlusive. . . sufficiently low to prevent desiccation of the wound, yet sufficiently high to prevent excessive accumulation of exudate below the wound **dressing**.
- SUMM In another embodiment, the wound **dressing** is fabricated in the form of dehydrated microparticles. These microparticles are especially suited to be applied into deep, highly exudative. . .
- The proposed polymer can also be used for the fabrication of a wound dressing containing one or more wound repair-promoting substances. Examples of such substances are for instance growth factors such as EGF, TGF-.alpha., FGFs, PDGFs, amphiregulin, HB-EGF, betacellulin, TGF-.beta., IGFs or other mitogens or their antagonists which may modulate the wound repair process. Such a medicated wound dressing can be produced in different forms, including flexible sheets, foams, microparticles, fibers to make up woven or non-woven tissues, etc. One of the embodiments of the invention concerns the production of a wound dressing containing multiple layers, where each layer contains a different active component, so as to achieve a programmed delivery of the. . .
- SUMM The present invention relates more particularly to the finding that GDP constitutes an excellent material for the preparation of dressings suitable for the covering and treatment of wounds. In addition, the material also displays unexpectedly favourable controlled release properties for. . .
- SUMM . . . polysaccharides useful within the framework of the invention. The molecular weight of the dextran used for the fabrication of wound dressings according to the invention is preferably below 5,000,000, more preferably between 10,000 and 100,000, in such a way that the. . .

SUMM

SUMM

SUMM

be used for the fabrication of a variety of wound **dressings**.

dehydration still takes place because fluid can evaporate from the surface of the film. To prevent this, the GDP wound **dressing** film can be additionally covered by one of the commercially available

the surface of the film. To prevent this, the GDP wound dressing film can be additionally covered by one of the commercially available occlusive or semi-occlusive wound dressing films, for example a polyurethane such as Opsite or Tegaderm. However, a better solution is provided according to another preferred. . . This type of film has a very low water vapour permeability, making it very suitable for the fabrication of wound dressings intended for use on relatively dry wounds. For application on more exudative wounds a higher evaporation rate is desirable, to prevent excessive accumulation of fluid under the dressing. In this instance, a backing membrane with higher water vapour permeability may be preferred, such as those manufactured by Utermohlen. . . shall be obvious that, depending on the type of wound, the degree of exudate formation and the desired frequency of dressing change, other backing films with different water vapour permeability properties can be used, to obtain an

optimal fluid balance at.

According to another embodiment, GDP is fabricated into a hydrated or dehydrated particulate wound dressing. Several techniques are known to achieve this. A dry GDP powder or granulate may be produced by dehydration of a. . . dehydrated gel particles, known to the person skilled in the art, may also be used to prepare a particulate wound dressing according to this invention. Such a particulate wound dressing may be useful for the treatment of a variety of wound types, but especially for the treatment of relatively deep. colonization, to the limitation of further necrotization and to the relieve of discomfort for the patient. Such a particulate wound dressing can also be used in its hydrated form (i.e. by omitting the dehydration process after particle preparation or by rehydrating. obvious that, depending on the needs of a particular wound type, the possibility also exists to use the particulate wound dressing in a partially hydrated form. In the latter form, the dressing still would have substantial fluid absorptive properties, yet, by virtue of a certain stickiness, it would easily be applicable as a paste or be fabricated into a thin film. By adapting the type of gel, wound dressings can be designed that are appropriate for treatment of other wounds such as corneal wounds or defects, tympanic membrane reconstructions,. . . chronic otorrhea. It shall also be clear that the dehydrated, partially hydrated and fully hydrated forms of these particulate wound dressings can be suspended in any suitable aqueous or organic excipient to facilitate application. Examples of such excipients include, but are.

SUMM

Another physical form into which GDP wound **dressings** can be fabricated is a foam. This can be achieved for instance by adding a suitable biocompatible detergent to the. . .

SUMM

. . . a known affinity for certain growth factors or wound healing-promoting substances. Examples of such components are those with affinity for heparin binding proteins, such as heparin or functional analogs of heparin such as heparan sulfate, chondroitin sulfate, dermatan sulfate, dextran sulfate or any other non-toxic polyanionic group displaying sufficient affinity for one or more of the molecular factors implicated in the. . . wound repair stimulating factors. These factors may subsequently be gradually released, thus promoting healing of the injury. The potential of heparin-like molecules and similar polyanions to bind and stabilize certain growth factors is well known in the art. The following are. . . Biophys., 300, p.30-41, 1993; Biochim. Biophys. Acta 1203, p.18-26, 1993). Tomoko et al. describe the stabilization of basic FGF

with dextran sulfate (FEBS Letters, 306, p.243-246, 1992). Turnbull and Gallagher review the role of heparan sulphate as a functional modulator of fibroblast growth factor activity (Biochem. Soc. Trans. 21, 477-482, 1993). By the incorporation of such polyanionic compounds in the GDP matrix. . .

SUMM One of the possible applications of the present invention lies in the fabrication of wound dressings containing one or more wound repair stimulating factors and/or a suitable antiseptic agent. Wound repair stimulating agents which are eligible for incorporation in such a wound dressing are for instance growth factors such as those belonging to the class of the EGF, FGF, PDGF, TGF-.beta., VEGF, PD-ECGF.

. agents include antibiotics, antibacterial sulfamides or peptides, chinolones, antimycotics, etc., as far as they are suitable for topical

chinolones, antimycotics, etc., as far as they are suitable for topical use. Wound dressings containing wound repair promoting agents can be used for the treatment of wounds which are difficult to heal. Injuries which. . . tympanic membrane perforations, surgical wounds, skin graft donor sites, burn wounds, etc. In the case of burn wounds, the wound dressings can be directly applied on a second or third degree burn. However, in case of extensive third degree burns, it is preferable to first graft the burn with meshed autologous skin. Application of the medicated GDP wound dressing directly on top of this autologous meshed graft will stimulate the closure of the meshed graft interstices, resulting in faster. . .

To facilitate application on the treatment site, the medicated GDP wound dressings can be manufactured in different forms. For instance, sheet- or film-like dressings can conveniently be applied onto burn wounds, shallow ulcers, skin graft donor sites and other types of shallow wounds. To reduce fluid evaporation and dehydration of the dressing and the underlying wound, the dressing can be covered with a flexible membrane, the water permeability of which is chosen so as to obtain an optimal. . . results from the atopic or superfluous presence of certain factors and that the presence of certain layers within the wound dressing can be used to sequester these unwanted factors. Other factors that can be sequestered comprise those that can lead to . . . also one of the advantages of the present invention that programmed delivery of several drugs is possible using

only one **dressing**, i.e. without having to change wound **dressings**.

SUMM . . . as some types of pressure sores or chronic ulcers, it may be more convenient to fabricate the medicated GDP wound **dressing** in the form of microparticles, foams, pastes or other forms which are easily conformable to the wound shape. Microparticles may. . .

SUMM It will be clear to the person skilled in the art that the fabrication of medicated wound **dressings** with controlled release properties is but one application of the present invention. Many other possible applications of the use of. . .

DETD . . . for instance Exkin (produced by Utermohlen NV, The Netherlands). This plastic foil, which can be used as a semi-occlusive wound dressing, has a bilayer structure consisting of a macroporous and a microporous layer. Due to its higher porosity, it has a. . .

DETD . . . X 1205 foil has a better barrier function and may thus be suited for the preparation of GDP laminate wound **dressings** intended for the treatment of wounds producing low amounts of exudate. On the contrary, the Exkin membrane allows a higher evaporation rate and is consequently more suited for preparation of GDP laminate wound **dressings** intended for the treatment of wounds producing high exudate volumes.

DETD One of the most important prerequisites for the clinical usefulness of a wound **dressing** is that it has a high biocompatibility.

- Therefore, it is essential that the material displays a very low or even. . $\ . \$
- DETD . . . on top of the methylcellulose gel covering the seeded cells. For comparison a similarly sized piece of the hydrocolloid ulcer dressing Duoderm (obtained from Convatec, UK) is placed on another well. A third well serves as negative control and receives no.

 . . and GDP, respectively. This indicates that GDP has a considerably lower cytotoxicity towards these fibroblasts than the commonly used ulcer dressing Duoderm.
- DETD . . . of surviving cells is 65 and 30% with GDP and Duoderm, respectively. After 6 days of incubation with the wound dressings, the percentage of surviving cells is 32 and 9% with GDP and Duoderm, respectively. This again confirms the superior cytotoxicity. . .
- DETD . . 1.4% of the cells survive with GDP and Duoderm, respectively.

 Once more, this underscores the superior properties of the GDP

 dressing, since it has only a limited cytotoxicity for

 keratinocytes, while incubation with Duoderm results in almost 100% cell

 death within. . .
- DETD . . . above show that GDP has a very favourable and low cytotoxicity level. We have compared GDP with Duoderm because both **dressings** are of a similar type and because the latter is a very frequently used **dressing** for the treatment of chronic ulcers. The fact that GDP is superior to Duoderm with respect to cytotoxicity underscores its clinical applicability as a wound **dressing**.
- DETD . . . inflammatory events or foreign body reactions are observed.

 This means the material is well suited for the fabrication of wound dressings.
- DETD . . . of Duoderm, while the remaining eight wounds serve as controls. All wounds are subsequently covered with Tegaderm (an occlusive polyurethane dressing) and fixed with Fixomull and Velpo bandages. At 2, 5, 9 and 20 days after surgery, two wounds of each treatment are examined macroscopically and subsequently fully. .
- DETD . . . GDP is a highly biocompatible material, which generates a significantly lower long term inflammatory response than the widely used ulcer **dressing** Duoderm. Moreover, the material is completely biodegradable over a period of 1-3 weeks, although it remains largely intact for about. . .
- DETD Preparation of a Polypeptide-loaded GDP Film
- DETD For evaluation of release kinetics of controlled delivery wound dressings, an elution test system as described above is not ideal. Since the elution is carried out by means of an. . . system can be considered as highly efficient, and with a kinetics profile which is suitable for application in a wound dressing.
- DETD For application in the manufacturing of growth factor-containing medicated wound **dressings**, GDP should also allow the efficient release of larger peptide factors. To evaluate this, a number of test proteins with. . .
- DETD . . . for larger proteins, release occurs with high efficiency and according to kinetics which are favourable for application in medicated wound **dressings**. Also, the stability of the matrix proves to be sufficient to allow prolonged storage.
- DETD . . . developing EGF for therapeutical purposes. Therefore, EGF can be regarded as an appropriate molecule to be incorporated in medicated wound **dressings** such as those disclosed in the present invention.
- DETD . . . bioactive form. GDP matrices according to this invention are therefore suitable controlled release devices for the fabrication of medicated wound **dressings**.

- DETD . . . pig model is conducted in order to further characterize and confirm the biocompatibility of dextran dialdehyde cross-linked gelatin hydrogel (GDP) dressing when placed in a full-thickness wound environment. The biocompatibility of GDP is evaluated, in comparison with two largely used dressings, the hydrocolloid dressing DuoDERM and the occlusive dressing Tegaderm, by characterization of the intensity and/or time duration of the inflammatory reaction during wound healing. A pilot study is. .
- DETD . . . containing 0.5% dextran sulphate (MW: 400000-600000), and 8 wounds are treated with extra thin DuoDERM (5 cm.times.5 cm), a hydrocolloid dressing from Convatec. All the wounds are covered with Tegaderm, an occlusive dressing which provides for a moist environment, and which is obtained from 3M Medical products. Dressings are fixed with Fixomull stretch, from Beiersdorf, and Velpo bandages to prevent possible self-trauma to the wounds.
- DETD T is the time given in days between the two wound healing evaluations. Since the **dressings** are not changed during this evaluation, A.sub.1 and P.sub.1 are the area and the perimeter of the wound at day.
- DETD . . . and Tegaderm treatments, indicating that GDP treatment is at least as good as two of the best and largely used dressings.

 Wounds treated with 0.5% dextran sulphate-containing GDP always appear in a more advanced stage of healing. For dextran sulphate-containing GDP-treated. . . radial progression towards wound closure is similar for three treatments (GDP, Tegaderm and Duoderm) indicating again that GDP is a dressing at least as good as Tegaderm or Duoderm, and certainly does not interfere negatively with wound healing. The radial progression. . .
- DETD . . . wound healing in pig, the healing of GDP-treated wounds is comparable to the healing of wounds treated with two good dressings (Duoderm and Tegaderm). The healing of the wounds treated with dextran sulphate-containing GDP is always in a more advanced stage. . .
- DETD . . . foreign body reaction is seen in the Duoderm-treated wounds. GDP and dextran sulphate-containing GDP can thus be considered as biocompatible dressings. In this example, dextran sulphate containing GDP-treated wounds re-epithelialize faster than DuoDERM and Tegaderm treated wounds indicating that dextran sulphate-containing.
- CLM What is claimed is:
 . antibody or a microprotein obtainable by phage display that have a high and selective affinity for molecular factors that can modulate the wound healing process.
 - 13. A medicament containing a biopolymer of claim 1 in the form of a wound **dressing** and/or controlled release device.

L52 ANSWER 5 OF 14 USPATFULL

2000:128306 USPATFULL ACCESSION NUMBER:

Chitin hydrogels, methods of their production and use TITLE: INVENTOR(S):

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NUMBER KIND DATE ________

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NUMBER DATE _____

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NUMBER OF DRAWINGS: 6 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 2441

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention is directed to the preparation and utilization of AB supplemented chitin hydrogels, such as chitosan hydrogels. Further provided are biomaterials comprising same. The particular supplement delivered by the chitin hydrogel is selected as a function of its intended use. In one embodiment, this invention provides a composition of matter, comprising a chitin hydrogel or chitin-derived hydrogel, wherein the hydrogel does not inhibit full-thickness skin wound healing.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L52 ANSWER 5 OF 14 USPATFULL

. . N.Y. pp. 231-277 (1979) and Brunt et al., Biotechnology 6:25-30 SUMM (1988)). These activities include recruiting cells, such as leukocytes and fibroblasts, into the injured area, and inducing cell proliferation and differentiation. Growth factors that may participate in wound healing include, but. . . growth factor-2 (IGF-2); epidermal growth factor (EGF); transforming growth factor-.alpha. (TGF-.alpha.); transforming growth factor-.beta. (TGF-.beta.); platelet factor 4 (PF-4); and heparin binding growth factors one and two (HBGF-1

and HBGF-2, respectively).

- The heparin binding growth factors (HBGFs), including the fibroblast growth factors (FGFs), which include acidic HBGF (aHBGF also known as HBFG-1 or FGF-1) and basic HBGF (bHBGF also known. . . Biochem. 58:575-606 (1989)). In addition, HBGF-1 is chemotactic for endothelial cells and astroglial cells. Both HBGF-1 and HBGF-2 bind to heparin, which protects them from proteolytic degradation. The array of biological activities exhibited by the HBGFs suggests that they play an. . .
- Demineralized bone matrix (DBM) is a source of osteoinductive proteins known as bone morphogenetic proteins (BMP), and growth factors which modulate the proliferation of progenitor bone cells (see, e.g., Hauschka et al., J. Biol. Chem. 261:12665-12674 (1986) and Canalis et al., . . .
- SUMM In another embodiment, this invention provides a simple to use, fast acting, field-ready bandage for applying a hydrogel to wounded tissue in a patient, comprising an occlusive backing, affixed to which is a layer. . . chitosan to produce a tissue-sealing hydrogel matrix upon hydration. Further embodiments pertain to the use and preparation of the chitin bandage.
- SUMM In yet another embodiment, this invention provides a simple to use, fast acting, field-ready dressing for treating wounded tissue in a patient, is formulated as an expandable foam comprising an effective amount of purified chitin. . . chitosan to produce a tissue-sealing hydrogel matrix upon hydration. Further embodiments pertain to the use and preparation of the chitin dressing.
- SUMM . . . that because the components of the chitin hydrogel can be formulated into several forms of simple to use, fast-acting field dressings, it is now possible to control bleeding from hemorrhaging trauma wounds, thereby saving numerous lives that previously would have been. . .
- DETD A "cross-linked chitin hydrogel" of the type used in the bandage or in the wound dressing of the present invention, refers to a hydrogel wherein the chitin component is cross-linked to form a stable matrix by. . .
- DETD . . . ulcers in diabetic individuals, and for delivering growth factors including, but not limited to, angiogenins; endothelins; hepatocyte growth factor and keratinocyte growth factor; fibroblast growth factors, including fibroblast growth factor-1 (FGF-1), fibroblast growth factor-2 (FGF-2), and fibroblast growth factor-4 (FGF-4); platelet-derived growth factors (PDGF); insulin-binding growth factors (IGF), including insulin-binding growth factor-1 and insulin-binding growth factor-2; epidermal. . . factor (OIF); osteogenin and other bone growth factors; bone morphogenetic growth factors (BMP), including BMP-1 and BMP-2; collagen growth factor; heparin-binding growth factors, including heparin-binding growth factor-1 and heparin -binding growth factor-2; cytokines; interferons; hormones and biologically active derivatives thereof, and providing a medium for prolonged contact between a wound. . .
- DETD . . . equivalent analogs thereof; colony stimulating factors; erythropoietin;; steroids; anesthetics; analgesics; and hormones. The above-mentioned drugs may be used to treat, reverse or prevent neoplasias, cell hyperproliferation. Neurotoxins, including antibiotics having neurotoxic effects such as gentamycin, may also be used to treat.
- DETD . . . be exploited to increase the duration of a drug's release from the hydrogel. Alternatively, this phenomenon can be exploited to modulate the release of drugs other than the compound used to stabilize the hydrogel, which is also incorporated into the

TET-hydrogel,. .

- DETD The chitin hydrogel may be formulated as a self-contained wound dressing, or bandage. The self-contained dressing or bandage is easy-to-use, requiring no advanced technical knowledge or skill to operate. It can even be self-administered as an emergency first. . .
- DETD The self-contained chitin hydrogel-containing wound dressing or bandage is an advancement over the current technology in that the field-ready preparation is inexpensive and can be stored for long. . .
- DETD The self-contained chitin hydrogel wound **dressing** or chitin hydrogel-containing **bandage** comprises a tissue sealing composition comprising a chitin hydrogel complex, which may consist of other chitins or their derivatives with. . .
- DETD The growth factor may include, e.g., fibroblast growth factor-1, fibroblast growth factor-2 and fibroblast growth factor-4; platelet-derived growth factor; insulin-binding growth factor-1; insulin-binding growth factor-2; epidermal growth factor; transforming growth factor-.alpha.; transforming growth factor-.beta.; cartilage-inducing factors -A and -B; osteoid-inducing factor; osteogenin and other bone growth factors; collagen growth factor; heparin-binding growth factor-1; heparin-binding growth factor-2; and/or their biologically active derivatives.
- DETD The concentration of the chitin hydrogel and/or hydrating agent(s) of the self-contained chitin hydrogel wound dressing or chitin hydrogel bandage may have a significant effect on the density and setting time of the final matrix. This principle may be used to satisfy specific uses of the self-contained chitin hydrogel-containing wound dressing or bandage in specialized situations.

 For example, the treatment of an arterial wound may require the chitin hydrogel seal to set very. . .
- DETD In the gel pack embodiment of the self-contained dressing, the chitin components and hydrating agent components are individually contained in independent quick-evaporating gel layers (e.g., methylcellulose/alcohol/water), wherein the two. . . from each other by an impermeable membrane, and the pair are covered with an outer, protective, second impermeable membrane. The bandage may be coated on the surface that is in contact with the gel in order to insure that the gel . .
- DETD . . . the two gel layers is removed, allowing the two components to mix. The outer membrane is then removed and the **bandage** is applied to the wound site. This results in a natural inhibition of blood and fluid loss from the wound, . . .
- DETD . . . chitin components and the hydrating agent, may be omitted. In operation, the outer impervious plastic film is removed and the bandage applied, as previously described, directly to the wound site. The fluids naturally present at the wound site then hydrate the.
- DETD The Chitin Hydrogel Bandage Embodiments
- DETD A chitin hydrogel bandage embodiment is formulated for releasing a necessary supplement to wounded tissue in a patient, wherein the bandage comprises, a layer of dry materials comprising an effective amount of chitin or its derivative to upon hydration form a hydrogel, wherein the layer of dry materials is affixed to the wound-facing surface of the bandage. In one embodiment, the occlusive backing and the physiologically-acceptable adhesive layer are one and the same, if the backing layer. . .
- DETD . . . a removable, waterproof, protective film is placed over the layer of dry materials and the exposed adhesive surface of the bandage for long-term stable storage. In operation the

waterproof, protective film is removed prior to the application of the bandage over the wounded tissue.

- DETD The chitin component of the bandage in one embodiment is activated at the time the bandage is applied to the wounded tissue to form a chitin hydrogel by the patient's endogenous fluids escaping from the hemorrhaging. . . chitin hydrogel is hydrated and fluid loss from the wound will be significantly diminished within minutes of application of the bandage to the wounded tissue. Although the speed with which the chitin hydrogel forms and sets may be to some degree. . . form within twenty minutes after application. More preferably, this effect will be evident within ten minutes after application of the bandage. Most preferably, the chitin hydrogel will form within two to five minutes after application. In the embodiment comprising the most. . .
- DETD It may be necessary to use pressure in applying the chitin hydrogel bandage until the chitin hydrogel has formed over the wound site.
- DETD . . . as in a life-threatening situation, the chitin hydrogel is hydrated by a suitable, physiologically-acceptable liquid prior to application of the **bandage** to the wounded tissue.
- DETD To construct the **bandage**, the dry materials may be obtained, for example, by lyophilization or freeze-drying, or suitable, commercially-available materials may be utilized. The. . .
- DETD The backing of the chitin hydrogel bandage may be of conventional, non-resorbable materials, e.g., a silicone patch or plastic material; or it may be of biocompatible, resorbable.
- DETD Subsequent removal of the clot with the backing is acceptable in many situations, such as when the chitin hydrogel **bandage** is used as a first aid measure until medical assistance becomes available.
- DETD . . . is advantageous to remove the backing from the chitin hydrogel without disturbing the established hydrogel matrix. Therefore, a chitin hydrogel bandage is provided in which the adhesive layer is of a material having a lower tensile or shear strength than that. . .
- DETD . . . comparison, certain internal applications mandate the use of a resorbable backing to eliminate the need for subsequent removal of the dressing. A resorbable material is one which is broken down spontaneously or by the body into components which are consumed or. .
- DETD . . . the chitin hydrogel. In the alterative for such purposes, the dry material layer may be affixed directly to the occlusive bandage.
- DETD . . . skin or tissue surrounding or adjacent to the wound in such a way that the dry material region of the **bandage** forms a chitin hydrogel directly over the wound. The adhesive layer on the region of backing which is not covered by the dry material layer of the **bandage** is sufficient to affix the chitin hydrogel to the tissue surrounding the wound until its physical removal. The adhesive on the outer region must be sufficient to hold the **bandage** in place, even if fluids are hemorrhaging from the wound under pressure, e.g., an arterial wound.
- DETD . . . the alterative for such purposes, the dry material layer may be affixed in the inner region directly to the occlusive **bandage**, with an adhesive layer added only to the outer layer.
- DETD Thus, in the two adhesive embodiment, the backing of the chitin hydrogel bandage remains in place affixed to the tissue surrounding the wound until the bandage is physically removed. But upon removal, the backing separates from the chitin hydrogel without disturbing matrix attached to the wound.
- DETD In yet another embodiment of the chitin hydrogel **bandage**, an independent hydrating layer comprising an effective amount of carbonated

water or physiologically-acceptable buffered hydrating agent, such as PBS, or. . . within a rupturable, liquid-impermeable container. The rupturable, liquid-impermeable container encapsulating the hydrating layer is affixed directly to the above-described occlusive bandage layer or to the above-described adhesive layer adjacent to the occlusive bandage. Affixed to the exposed side (the side which is not attached to the backing or adhesive layer) of the rupturable, . . .

- DETD . . . components until a malleable hydrated chitin hydrogel complex forms, at which time the outer membrane is physically removed and the bandage placed over the wound.
- DETD As in other embodiments of the chitin hydrogel bandage, the selected adhesives and backing materials may be determined by the intended application of the bandage. The backing may be removable or resorbable, and the adhesive may have the intended purpose upon removal of the bandage of removing the chitin hydrogel from the wound, or of leaving the chitin hydrogel undisturbed. The adhesive may be a. . .
- DETD . . . previously disclosed growth factors, antibiotics, antiseptics, antiproliferative drugs, etc. may also be included in this embodiment of the chitin hydrogel **bandage**.
- DETD In an alternate dual layer embodiment, the chitin hydrogel is delivered as a wound sealing **dressing**, which need not be affixed to a backing. The components are organized essentially as a capsule within a capsule, wherein. . .
- DETD A self-foaming chitin hydrogel **dressing** embodiment for treating wounded tissue in a patient is formulated as an expandable foam comprising a hydrogel-forming amount of chitin.
- DETD For example, use of the expandable foam chitin hydrogel dressing within the abdomen provides a chitin hydrogel to provide a barrier to infection while releasing a necessary supplement. However, at. . . harmful pressure on undamaged tissue, organs or blood vessels. Such a situation may warrant the use of an expandable foam dressing in which the expansion is limited to only 1- or 2-fold, and not more than 5-10 fold.
- DETD By comparison, use of the expandable foam chitin hydrogel dressing to fill gaps within bone, may warrant the use of material which expands at a much greater rate to produce.
- DETD Like the expansion rate, the set-up time for the formation of the chitin hydrogel using the expandable foam chitin hydrogel **dressing** is also related to its intended application. Although a set-up time of under 1 minute is appropriate, set-up times of. . .
- DETD Since delivery pressure of the expandable foam chitin hydrogel dressing from the delivery device, when combined with the composition of the chitin hydrogel itself and its set-up time, determines the extent of expansion of the dressing, the delivery pressure is determined by the nature of the wound being treated. Pressure of 1 atmosphere, or less (14.7. . .
- Finally, certain traumatic injuries will be best treated by combining several embodiments of the chitin hydrogel dressing. For example, in serious car accidents or injuries caused by antipersonnel-mines or explosives, the wounds may be not only life-threatening. . . first liberally apply a hemostatic agent, and then to wrap the entire area in an embodiment of the chitin hydrogel bandage to support and protect the wounded area, and perhaps release a painkilling and/or antimicrobial composition and slow fluid loss with. . . to a medical facility, or until professional medical assistance can administered. In most instances, additional formulations of the chitin hydrogel dressing will then be applied by the trained personnel for the long-term repair, treatment and protection of

the injured tissue.

DETD . . . can be stabilized using ionic crosslinking with positively charged polypeptides (Singh, M., Ph.D. Thesis: "Electrostatic effects on the release of polypeptides from collagen hydrogels ," Univ. of Maryland, Baltimore County, Baltimore, Md. (1994)). This current work supports the earlier study as evidenced by the fact. . . DETD . . . decreased by combining negatively charged NOCC with positively charged polylysine (PL) (Singh M., Ph.D. Thesis: Electrostatic effects on release of polypeptides from collagen hydrogels, Univ. of Maryland, Baltimore, Md. (1994)) to retard the diffusional mobility of the diffusing species. The present example discloses the. .

CLM What is claimed is:
25. A wound **dressing** composition for treatment of wounded tissue, said composition comprising a covalently cross-linked N,O-carboxymethyl chitosan hydrogel; and a resorbable backing consisting. . .

L52 ANSWER 6 OF 14 USPATFULL

ACCESSION NUMBER: 1999:92656 USPATFULL

TITLE: Compositions and methods for modulating

growth of a tissue in a mammal

INVENTOR(S): Weisz, Paul B., State College, PA, United States

PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania,

Philadelphia, PA, United States (U.S. corporation)

| | NUMBER | | KIND | DATE |
|---------------------|--------|-------------|------|----------|
| | | | | |
| PATENT INFORMATION: | US | 5935940 | | 19990810 |
| APPLICATION INFO.: | US | 1997-906500 | | 19970805 |

RELATED APPLN. INFO.: Division of Ser. No. US 1994-345011, filed on 23 Nov

1994, now patented, Pat. No. US 5658894 which is a continuation of Ser. No. US 1992-900592, filed on 18 Jun 1992, now abandoned And a continuation-in-part of Ser. No. US 1991-790320, filed on 12 Nov 1991, now abandoned which is a continuation of Ser. No. US 1991-691168, filed on 24 Apr 1991, now abandoned which

1991-691168, filed on 24 Apr 1991, now abandoned which is a continuation of Ser. No. US 1989-397559, filed on 23 Aug 1989, now abandoned , said Ser. No. US 900592

which is a continuation-in-part of Ser. No. US 1990-480407, filed on 15 Feb 1990, now patented, Pat.

No. US 5183809

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Lee, Howard C.

LEGAL REPRESENTATIVE: Panitch Schwarze Jacobs & Nadel, P.C.

NUMBER OF CLAIMS: 29 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 6 Drawing Figure(s); 5 Drawing Page(s)

LINE COUNT: 1497

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Polyionic derivatives of cyclodextrins and methods for preparing these derivatives are provided in which a polyionic derivative of cyclodextrin is combined with a growth factor, preferably a heparin binding growth factor. These compositions are of low solubility and are applied directly to the location of a wound. By virtue of the low solubility, the compositions remain in place at the site of application and slowly release growth factor. In an alternative embodiment, the cyclodextrin derivatives are administered in the absence of growth factor and are used to absorb growth factor present in the body at the location of the wound in order to prevent overstimulation of the wound response.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 6

L52 ANSWER 6 OF 14 USPATFULL

TI Compositions and methods for **modulating** growth of a tissue in a mammal

DETD . . . thus be introduced at or near the sites of tissue damage or sites of implantation, or applied externally as wound **dressings** , etc. In such embodiments, the compositions and compounds of the present invention are preferably combined with a solid carrier which. .

- DETD . . . and/or are combined with biologically active proteins.

 According to preferred embodiments, the biologically active protein exhibits a specific affinity for heparin, and, more specifically, is heparin-binding growth factor, i.e., a class of growth factors, many of which are mitogenic for endothelial cells. An example of such a growth factor is basic fibroblast growth factor. Generally it will be the heparin-binding growth factor proteins, commonly referred to as HBGF's, which may be combined with the saccharide derivatives of the present invention. . .
- DETD . . . shift resulting from heparin binding on the dye has been used to identify active heparin-like compounds having the capability of modulating angiogenesis. Such dye complexing of the active protein also is similarly resistant to salt concentration as is the complexing to. . .
- DETD . . . example of a flat polymer product of polyamide polymer, manufactured by 3M Corporation, and used as a bio-compatible patch or dressing on wounds. This biocompatible patch or dressing is designed to physically protect a wound from invasion of pathogens, and yet to have sufficient porosity to allow passage. . . or already present in biomembranes. Biological membranes such as omentum and amnion are well known in the art as wound dressings. Collagen based synthetic biomembranes are being used in the treatment of burns. The presence of derivatized saccharide of the present. . .
- DETD . . . (1952, J. Biol. Chem. 193:265-275). Protein concentrations of the pure growth factor were estimated by comparing the intensities of silver-stained **polypeptide** bands of SDS-polyacrylamide **gel** to those of the molecular weight markers.
- DETD . . . NaCl, about 230 units of three activity was recovered when eluted with about 2M NaCl. These results indicate that basic fibroblast growth factor has a very strong affinity for beta-cyclodextrin tetradecasulfate and is at least comparable to that of FGF for heparin. The activity peak was analyzed by SDS polyacrylamide gel electrophoresis followed by a silver stain. Lane 2 in FIG. 4 shows the polypeptide band of basic fibroblast growth
- CLM What is claimed is:
 - 1. A composition for **modulating** growth of a tissue of a mammal, the composition comprising a growth-**modulating** polyanionic cyclodextrin derivative monomer, wherein said monomer comprises at least six glucopyranose units and at least two, but fewer than. . .
 - 20. The composition of claim 19, wherein said heparin binding growth factor is selected from the group consisting of brain endothelial cell growth factor, retina-derived growth factor, interleukin-1, interleukin-2, interferon alpha, interferon gamma, tumor necrosis factor alpha, epidermal growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, insulin-like growth factor-1, insulin-like growth factor-2, platelet-derived growth factor, transforming growth factor-alpha, and transforming growth factor-beta.
 - . a medium comprising a growth factor, the method comprising the steps of contacting said medium with a composition comprising a growth-modulating polyanionic cyclodextrin derivative monomer under conditions which permit binding of said growth factor to said composition, wherein said monomer comprises. . .

L52 ANSWER 7 OF 14 USPATFULL

1999:56471 USPATFULL ACCESSION NUMBER:

TITLE: Methods of modulating tissue growth and

regeneration

Herrmann, Howard C., Bryn Mawr, PA, United States INVENTOR(S):

Barnathan, Elliot, Havertown, PA, United States Weisz, Paul B., State College, PA, United States

The Trustees of the University of Pennsylvania, PATENT ASSIGNEE(S):

Philadelphia, PA, United States (U.S. corporation)

NUMBER KIND DATE US 5902799 US 1997-906501 19990511 PATENT INFORMATION:

APPLICATION INFO.: 19970805 (8) Division of Ser. No. US 1994-345011, filed on 23 Nov RELATED APPLN. INFO.:

1994, now patented, Pat. No. US 5658894 which is a continuation of Ser. No. US 1992-900592, filed on 18

Jun 1992, now abandoned And a continuation-in-part of Ser. No. US 1991-790320, filed on 12 Nov 1991, now abandoned which is a continuation of Ser. No. US

1991-691168, filed on 24 Apr 1991, now abandoned which is a continuation of Ser. No. US 1989-397559, filed on 23 Aug 1989, now abandoned , said Ser. No. US 900592

which is a continuation-in-part of Ser. No. US

1990-480407, filed on 15 Feb 1990, now patented, Pat.

No. US 5183809

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

Lee, Howard C. PRIMARY EXAMINER:

Panitch Schwarze Jacobs & Nadel, P.C. LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 6 Drawing Figure(s); 5 Drawing Page(s)

1703 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Polyionic derivatives of cyclodextrins and methods for preparing these derivatives are provided in which a polyionic derivative of cyclodextrin is combined with a growth factor, preferably a heparin binding growth factor. These compositions are of low solubility and are applied directly to the location of a wound. By virtue of the low solubility, the compositions remain in place at the site of application and slowly release growth factor. In an alternative embodiment, the cyclodextrin derivatives are administered in the absence of growth factor and are used to absorb growth factor present in the body at the location of the wound in order to prevent overstimulation of the wound response.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 7

L52 ANSWER 7 OF 14 USPATFULL

TI Methods of modulating tissue growth and regeneration

. . . thus be introduced at or near the sites of tissue damage or sites of implantation, or applied externally as wound dressings , etc. In such embodiments, the compositions and compounds of the present invention are preferably combined with a solid carrier which.

- DETD . . . and/or are combined with biologically active proteins.

 According to preferred embodiments, the biologically active protein exhibits a specific affinity for heparin, and, more specifically, is heparin-binding growth factor, i.e., a class of growth factors, many of which are mitogenic for endothelial cells. An example of such a growth factor is basic fibroblast growth factor. Generally it will be the heparin-binding growth factor proteins, commonly referred to as HBGF's, which may be combined with the saccharide derivatives of the present invention. . .
- DETD . . . shift resulting from heparin binding on the dye has been used to identify active heparin-like compounds having the capability of modulating angiogenesis. Such dye complexing of the active protein also is similarly resistant to salt concentration as is the complexing to. . .
- DETD . . . example of a flat polymer product of polyamide polymer, manufactured by 3M Corporation, and used as a bio-compatible patch or dressing on wounds. This biocompatible patch or dressing is designed to physically protect a wound from invasion of pathogens, and yet to have sufficient porosity to allow passage. . . or already present in biomembranes. Biological membranes such as omentum and amnion are well known in the art as wound dressings. Collagen based synthetic biomembranes are being used in the treatment of burns. The presence of derivatized saccharide of the present. . .
- DETD . . . (1952, J. Biol. Chem. 193:265-275). Protein concentrations of the pure growth factor were estimated by comparing the intensities of silver-stained **polypeptide** bands of SDS-polyacrylamide **gel** to those of the molecular weight markers.
- DETD . . . NaCl, about 230 units of the activity was recovered when eluted with about 2M NaCl. These results indicate that basic **fibroblast** growth factor has a very strong affinity for beta-cyclodextrin tetradecasulfate and is at least comparable to that of FGF for **heparin**. The activity peak was analyzed by SDS polyacrylamide gel electrophoresis followed by a silver stain. Lane 2 in FIG. 4 shows the polypeptide band of basic **fibroblast** growth factor.

 CLM What is claimed is:
 - . cell growth factor, retina-derived growth factor, interleukin-1, interleukin-2, interferon alpha, interferon gamma, tumor necrosis factor alpha, epidermal growth factor, acidic **fibroblast** growth factor, basic **fibroblast** growth factor, insulin-like growth factor-1, insulin-like growth factor-2, platelet-derived growth factor, transforming growth factor-alpha, transforming growth factor-beta, and a **heparin**-binding growth factor.
 - 30. The method of claim 29, wherein the growth factor is selected from the group consisting of brain endothelial cell growth factor, retina-derived growth factor, interleukin-1, interleukin-2, interferon alpha, interferon gamma, tumor necrosis factor alpha, epidermal growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, insulin-like growth factor-1, insulin-like growth factor-2, platelet-derived growth factor,

transforming growth factor-alpha, transforming growth factor-beta, and a heparin-binding growth factor.

- 45. The method of claim 44, wherein the growth factor is selected from the group consisting of interleukin-1, interleukin-2, interferon alpha, interferon gamma, tumor necrosis factor alpha, epidermal growth factor, acidic **fibroblast** growth factor, basic **fibroblast** growth factor, insulin-like growth factor-1, insulin-like growth factor-2, platelet-derived growth factor, transforming growth factor-alpha, transforming growth factor-beta, and a **heparin** -binding growth factor.
- 60. A method of modulating proliferation of an endothelial cell in a mammal, the method comprising administering locally to the endothelial cell a composition comprising a polyanionic cyclodextrin derivative and a physiologically acceptable carrier in an amount effective to modulate proliferation of the endothelial cell, the cyclodextrin derivative comprising at least one cyclodextrin monomer and having a body temperature solubility. 61. The method of claim 60, wherein modulating proliferation of an endothelial cell comprises promoting proliferation of the endothelial cell, and wherein the composition frrther comprises a growth. . . selected from the group consisting of interleukin-1, interleukin-2, interferon alpha, interferon gamma, tumor necrosis factor alpha, epidermal growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, insulin-like growth factor-1, insulin-like growth factor-2, platelet-derived growth factor, transforming growth factor-alpha, transforming growth factor-beta, and a heparin-binding growth factor.
- 62. The method of claim 60, wherein **modulating** proliferation of an endothelial cell comprises inhibiting proliferation of the endothelial cell.

L52 ANSWER 9 OF 14 USPATFULL

ACCESSION NUMBER: 1998:115708 USPATFULL

TITLE: Heparin binding mitogen with homology to epidermal

growth factor (EGF)

INVENTOR(S): Klagsbrun, Michael, Newton, MA, United States

Abraham, Judith A., San Jose, CA, United States

Higashiyama, Shigeki, Osaka, Japan

Besner, Gail E., Buffalo, NY, United States

PATENT ASSIGNEE(S): The Childrens Medical Center Corp., Boston, MA, United

States (U.S. corporation)

Scios Nova, Inc., Mountain View, CA, United States

(U.S. corporation)

| • | NUMBER | KIND DATE | |
|---|---|-----------|----------------------------------|
| PATENT INFORMATION: APPLICATION INFO.: | US 5811393 US 1993-39364 WO 1991-US7691 | | (8) PCT 371 date PCT 102(e) date |

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1990-598082, filed

on 16 Oct 1990, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted

PRIMARY EXAMINER: Allen, Marianne P. LEGAL REPRESENTATIVE: Fish & Richardson P.C.

NUMBER OF CLAIMS: 24 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)

LINE COUNT: 1650

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are heparin binding mitogens which include an epidermal growth factor-homologous segment (HB-EHM). These factors stimulate proliferation of fibroblast cells, epithelial cells, and smooth muscle cells, but not endothelial cells. Also disclosed are isolated antibodies that recognize, and purified nucleic acids that encode, the above growth factors as well as isolated polypeptides, vectors containing such nucleic acids, and cells harboring such vectors. Growth factors of this invention may be used for accelerating the rate of wound healing, for the in vitro culture of HB-EHM-responsive cells, and for the identification of antagonists to HB-EHM.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L52 ANSWER 10 OF 14 USPATFULL

ACCESSION NUMBER: 97:73601 USPATFULL

Compositions for inhibiting restenosis TITLE:

Weisz, Paul B., State College, PA, United States The Trustees of the University of Pennsylvania, INVENTOR(S):

PATENT ASSIGNEE(S): Philadephia, PA, United States (U.S. corporation)

> DATE NUMBER KIND ______

US 5658894 PATENT INFORMATION: US 1994-345011 19970819 APPLICATION INFO.: 19941123 (8)

Continuation of Ser. No. US 1992-900592, filed on 18 RELATED APPLN. INFO.:

Jun 1992, now abandoned And a continuation-in-part of Ser. No. US 1991-790320, filed on 12 Nov 1991, now abandoned which is a continuation-in-part of Ser. No. US 1991-691168, filed on 24 Apr 1991, now abandoned which is a continuation of Ser. No. US 1989-397559, filed on 23 Aug 1989, now abandoned , said Ser. No. US -900592 which is a continuation-in-part of Ser. No. US 1990-480407, filed on 15 Feb 1990, now patented, Pat.

No. US 5183809, issued on 2 Feb 1993

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

Wityshyn, Michael G. PRIMARY EXAMINER: Prats, Francisco C. ASSISTANT EXAMINER:

Panitch Schwarze Jacobs & Nadel, P.C. LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: 14 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 6 Drawing Figure(s); 5 Drawing Page(s)

LINE COUNT: 1449

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Polyionic derivatives of cyclodextrins and methods for preparing these AB derivatives are provided in which a polyionic derivative of cyclodextrin is combined with a growth factor, preferably a heparin binding growth factor. These compositions are of low solubility and are applied directly to the location of a wound. By virtue of the low solubility, the compositions remain in place at the site of application and slowly release growth factor. In an alternative embodiment, the cyclodextrin derivatives are administered in the absence of growth factor and are used to absorb growth factor present in the body at the location of the wound in order to prevent overstimulation of the wound response.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 10

L52 ANSWER 10 OF 14 USPATFULL

. . . thus be introduced at or near the sites of tissue damage or DETD sites of implantation, or applied externally as wound dressings , etc. In such embodiments, the compositions and compounds of the present invention are preferably combined with a solid carrier which.

. and/or are combined with biologically active proteins. According to preferred embodiments, the biologically active protein exhibits a specific affinity for heparin, and, more specifically, is heparin-binding growth factor, i.e., a class

of growth factors, many of which are mitogenic for endothelial cells. An example of such a growth factor is basic **fibroblast** growth factor. Generally it will be the **heparin**-binding growth factor proteins, commonly referred to as HBGF's, which may be combined with the saccharide derivatives of the present invention....

- DETD . . . shift resulting from heparin binding on the dye has been used to identify active heparin-like compounds having the capability of modulating angiogenesis. Such dye complexing of the active protein also is similarly resistant to salt concentration as is the complexing to. . .
- DETD . . . example of a flat polymer product of polyamide polymer, manufactured by 3M Corporation, and used as a bio-compatible patch or dressing on wounds. This biocompatible patch or dressing is designed to physically protect a wound from invasion of pathogens, and yet to have sufficient porosity to allow passage. . . or already present in biomembranes. Biological membranes such as omentum and amnion are well known in the art as wound dressings. Collagen based synthetic biomembranes are being used in the treatment of burns. The presence of derivatized saccharide of the present. . .
- DETD . . . J. Biol. Chem. 193: 265-275). Protein concentrations of the pure growth factor were estimated by comparing the intensities of silver-stained **polypeptide** bands of SDS-polyacrylamide **gel** to those of the molecular weight markers.
- DETD . . . NaCl, about 230 units of the activity was recovered when eluted with about 2M NaCl. These results indicate that basic **fibroblast** growth factor has a very strong affinity for beta-cyclodextrin tetradecasulfate and is at least comparable to that of FGF for heparin. The activity peak was analyzed by SDS polyacrylamide gel electrophoresis followed by a silver stain. Lane 2 in FIG. 4 shows the polypeptide band of basic **fibroblast** growth factor.
- CLM What is claimed is:
 7. The composition of claim 6 wherein the heparin binding growth factor is fibroblast growth factor.

=> d ibib abs kwic 11

L52 ANSWER 11 OF 14 USPATFULL

ACCESSION NUMBER: 93:74208 USPATFULL

TITLE: Polypeptides for adhering cells to a substrate

INVENTOR(S): Tsilibary, Effie C., Minneapolis, MN, United States

Furcht, Leo T., Minneapolis, MN, United States

Regents of the University of Minnesota, Minneapolis, PATENT ASSIGNEE(S):

MN, United States (U.S. corporation)

NUMBER KIND DATE PATENT INFORMATION: US 5242826 19930907 APPLICATION INFO.: US 1991-705086 19910524 (7) 20061024 DISCLAIMER DATE:

RELATED APPLN. INFO.: Division of Ser. No. US 1991-648190, filed on 31 Jan

> 1991, now patented, Pat. No. US 5059425 which is a division of Ser. No. US 1989-397012, filed on 22 Aug 1989, now patented, Pat. No. US 5007925 which is a division of Ser. No. US 1987-106858, filed on 8 Oct

1987, now patented, Pat. No. US 4876332

DOCUMENT TYPE: Utility Granted FILE SEGMENT: PRIMARY EXAMINER: Naff, David M.

Merchant, Gould, Smith, Edell, Welter & Schmidt LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 24 Drawing Figure(s); 12 Drawing Page(s)

LINE COUNT: 618

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A polypeptide which can bind heparin and promote cellular adhesion is provided, which consists essentially of a polypeptide having a formula selected from the group consisting of:

met-phe-lys-lys-pro-thr-pro-ser-thr-leu-lys-ala-gly-glu-leu-arg,

thr-ala-gly-ser-cys-leu-arg-lys-phe-ser-thr met,

asn-pro-leu-cys-pro-pro-gly-thr-lys-ile-leu,

and mixtures thereof.

Medical devices such as prosthetic implants, percutaneous devices, bandages and cell culture substrates coated with the polypeptide composition are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Medical devices such as prosthetic implants, percutaneous devices, AB bandages and cell culture substrates coated with the polypeptide composition are also provided.

Lyophilized crude polypeptides are purified by preparative high DETD performance liquid chromatography (HPLC) by reverse phase technique on a C-18 column. A typical elution gradient is 0% to 60% acetonitrile with 0.1% TFA in H.sub.2. .

In summary, peptide TS-1 promotes adhesion of aortic endothelial cells, DETD metastatic carcinoma M.sub.4 cells, normal rat fibroblasts, MM fibrosarcoma cells, C6 glioma cells and A431 breast carcinoma cells. Peptide TS-2 binds (a) to type IV collagen, (b) to heparin and (c) promotes adhesion of the above-mentioned cell lines. Peptide TS-3

- (a) binds to **heparin** and (b) promotes adhesion of the above-mentioned cell lines.
- DETD . . . in particular may be strongly attracted to the present polypeptides. The latter point indicates the potential usefulness of these defined **polypeptides** in **coating** a patch graft or the like for aiding wound closure and healing following an accident or surgery.
- DETD . . . used to coat the surface of medical devices intended for external application of attachment to the body. Such devices include "bandages", which term is also intended to refer to wound packs and dressings, which can comprise surfaces formed from absorbent cellulosic fibers, from synthetic fibers or from mixtures thereof. These surfaces can be. . .

=> d ibib abs kwic 12

L52 ANSWER 12 OF 14 USPATFULL

ACCESSION NUMBER: 91:86566 USPATFULL

TITLE: Bandage comprising a fibrous surface coated

with polypeptides with type IV collagen activity
INVENTOR(S): Tsilibary, Effie C., Minneapolis, MN, United States

Furcht, Leo T., Minneapolis, MN, United States

PATENT ASSIGNEE(S): Regents of the University of Minnesota, Minneapolis,

MN, United States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5059425 19911022 APPLICATION INFO.: US 1991-648190 19910131 (7)

RELATED APPLN. INFO.: Division of Ser. No. US 1989-397012, filed on 22 Aug

1989, now patented, Pat. No. US 5007925 which is a division of Ser. No. US 1987-106858, filed on 8 Oct

1987, now patented, Pat. No. US 4876332

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lee, Mary C.

ASSISTANT EXAMINER: Ambrose, Michael G.

LEGAL REPRESENTATIVE: Merchant, Gould, Smith, Edell, Welter & Schmidt

NUMBER OF CLAIMS: 2

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 21 Drawing Figure(s); 12 Drawing Page(s)

LINE COUNT: 613

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A composition which can bind heparin and promote cellular adhesion is provided which consists essentially of a polypeptide of the formula:

met-phe-lys-lys-pro-thr-pro-ser-thr-leu-lys-ala-qly-qlu-leu-arg,

thr-ala-gly-ser-cys-leu-arg-lys-phe-ser-thr-met,

asn-pro-leu-cys-pro-pro-gly-thr-lys-ile-leu,

or mixtures thereof.

Medical devices such as prosthetic implants, percutaneous devices, bandages and cell culture substrates coated with the polypeptide composition are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Bandage comprising a fibrous surface coated with polypeptides with type IV collagen activity

AB Medical devices such as prosthetic implants, percutaneous devices, bandages and cell culture substrates coated with the polypeptide composition are also provided.

DETD Lyophilized crude polypeptides are purified by preparative high performance liquid chromatography (HPLC) by reverse phase technique on a C-18 column. A typical elution gradient is 0% to 60% acetonitrile with 0.1% TFA in H.sub.2. . .

DETD In summary, peptide TS-1 promotes adhesion of aortic endothelial cells, metastatic carcinoma M.sub.4 cells, normal rat fibroblasts, MM fibrosarcoma cells, C6 glioma cells and A431 breast carcinoma cells. Peptide TS-2 binds (a) to type IV collagen, (b) to heparin and (c) promotes adhesion of the above-mentioned cell lines. Peptide TS-3

- (a) binds to **heparin** and (b) promotes adhesion of the above-mentioned cell lines.
- DETD . . . in particular may be strongly attracted to the present polypeptides. The latter point indicates the potential usefulness of these defined **polypeptides** in **coating** a patch graft or the like for aiding wound closure and healing following an accident or surgery.
- DETD . . . used to coat the surface of medical devices intended for external application or attachment to the body. Such devices include "bandages", which term is also intended to refer to wound packs and dressings, which can comprise surfaces formed from absorbent cellulosic fibers, from synthetic fibers or from mixtures thereof. These surfaces can be. . .
- CLM What is claimed is:

 1. A bandage comprising a fibrous surface coated with a polypeptide consisting essentially of: met-phe-lys-lys-pro-thr-pro-ser-thr-leu-lys-ala-gly-glu-leu-arg, thr-ala-gly-ser-cys-leu-arg-lys-phe-ser-thr-met, asn-pro-leu-cys-pro-pro-gly-thr-lys-ile-leu, or mixtures thereof.
 - 2. The **bandage** of claim 1 wherein the fibrous surface comprises cellulosic fibers.